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Early Recurrence Following Intravitreal Ranibizumab Versus Aflibercept for Treatment of Egyptian Diabetic Macular Edema

Alaa Hussien Abotaleb
ophthalmology, Elhelal Hospital, Sohag, Egypt

Shaimaa Mamdouh Mostafa
ophthalmology, Faculty of Medicine, Al-Azhar University, Assiut, Egypt, shimaa.mamdouh@azhar.edu.eg

Emad Abdel-Aal Saliem
ophthalmology, Faculty of Medicine, Al-Azhar University, Assiut, Egypt

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ORIGINAL ARTICLE

Early Recurrence Following Intravitreal Ranibizumab Versus Aflibercept for Treatment of Egyptian Diabetic Macular Edema

Alaa H. Abotaleb [a], Shaimaa M. Mostafa [b,*], Emad A. Saliem[b]

[a] Department of ophthalmology, Elhelal Hospital, Sohag, Egypt
[b] Department of ophthalmology, Faculty of Medicine, Al-Azhar University, Assiut, Egypt

Abstract

Background: ***Diabetic macular edema (DME) is one of the most common causes of vision loss.***

Aim: ***To compare the early recurrence in terms of clinical outcomes and structural alterations in the retina following intravitreal injections of the anti-VEGFs ranibizumab and aflibercept for the treatment of diabetic macular edema.***

Patients and Methods: ***A prospective, interventional, comparative, randomized clinical study with 100 eyes was conducted. The subjects were split into two groups: the ranibizumab group (50 eyes) and the aflibercept group (50 eyes).***

Results: ***Regarding the total study population, the intergroup comparison revealed a significant difference at the first-month follow-up with more improvement of BCVA in the IVA group (p=0.01) and no significant difference at the third-month follow-up (p=0.59). However, there was a highly significant difference at the sixth-month follow-up in favor of the IVA group (p=0.0001). As regards CMT, The intergroup comparison of CMT values indicated more improvement in the IVA group over the IVR group, which was statistically significant in the first month (p= 0.002) and highly significant in the sixth-month visit (p<0.0001) respectively), However, there was no statistically significant difference at the third-month visit (P=0.48).***

Conclusion ***Aflibercept and ranibizumab were effective in treating DME. Aflibercept, nevertheless, produced more stable results in terms of morphology and vision.***

Keywords: Optical coherence tomography; Anti Vascular Endothelial Growth Factor (VEGF); Intravitreal injection; CMT

1. Introduction

Diabetic macular edema (DME) is one of the most common causes of vision loss. Because of changes in fine penetrability,[1] it appears as a thickening of the retina.[2] When the retinal micro-vasculature is damaged, the blood-retina barrier breaks down, which encourages the synthesis of VEGF and causes edema.[3]

While treating focal diabetic macular edema (DME), intravitreal infusion (IVI) against VEGFs is often used as the main line of treatment since it has been displayed to lessen DME and upgrade vision in DME-impacted eyes.[4]

Hostile to VEGF prescriptions, ranibizumab, and aflibercept has been authorized for use in the treatment of DME. A monoclonal immunizer piece called ranibizumab kills all VEGF-An isoforms. Aflibercept is a recombinant combination protein comprising of human VEGFR-1 and VEGFR-2 extracellular space parts melded to the human immunoglobulin G1 Fc subunit. It is strongly receptive to all VEGF-A isoforms, VEGF-B, and placental growth factor (PGF) .[5]

Therefore, this study aims to compare the stability of visual acuity and CMT following intravitreal injection of ranibizumab and aflibercept, anti-VEGFs, in patients with diabetic macular edema (DME).

2. Patients and methods

100 eyes of 76 DME patients, with two eyes included in 24 patients and one eye included in 52 patients. Aflibercept was injected intravitreally into 50 eyes (IVA group), while ranibizumab was injected intravitreally into 50 additional eyes (IVR group).

Patients were gathered from the ophthalmology department of el-helal Sohag Health Insurance Hospital and Al Azhar University Assiut Hospital; All participants gave their consent. Approval of the Ethical Committee of the Faculty of Medicine in Al Azhar University Assiut Hospital was attained.

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* Corresponding author at: ophthalmology, Faculty of Medicine, Al-Azhar University, Assiut, Egypt.
E-mail address: shimaa.mamdouh@azhar.edu.eg (S. M. Mostafa).

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The entire process was carried out in conformity with the institutional committee's ethical guidelines, the 1964 Helsinki Declaration and its later revisions, or other comparable ethical guidelines. Informed approval: All individuals involved in the study gave their informed consent.

Patients who neglected to finish the development and those with uncontrolled diabetes were wiped out from the preliminary. We started with 150 eyes altogether. To evaluate the progressions in macular thickness and visual keenness after intravitreal infusion of aflibercept or ranibizumab regulated in patients giving diabetic macular edema (DME), 100 eyes were enrolled in the study. They were divided into two groups:

IVA Group (50 eyes): received intravitreal aflibercept injection 2 mg (0.05 ml of 40 mg/ml solution).

IVR Group (50 eyes): The patient received an intravitreal ranibizumab injection of 0.5 mg (0.05 ml of 10 mg/ml solution). The dose was 0.05 ml of the drug.

All patients of the two gatherings had gotten three infusions within a month with a trail behind the first and third infusions, and no extra portions were given. Then, at that point, follow-up was finished multiple months after the last injection. Diabetic macular edema was identified in this study when a patient's best corrected visual acuity (BCVA) was less than 20/40, and their central macular thickness was greater than 280 m. Patients with macular edema brought about by conditions other than diabetes, patients who had gone through visual medical procedures in the past half a year, glassy discharge, uncontrolled glaucoma, and media opacities that essentially decreased BCVA were likewise barred from the review.

In order to maintain strict asepsis, intravenous injections of aflibercept and ranibizumab were given in the operating room. Draping and a sterile eyelid speculum were applied following the application of benoxinate HCL drops and povidone-iodine solution for topical anesthesia. For phakic eyes, intravitreal injections were given with a 30-gauge needle 4 mm posterior to the limbus and 3.5 mm for pseudophakic eyes. The initial examination included a comprehensive medical history and an extensive ophthalmologic examination, including fundus fluorescein angiography (FFA), slit lamp biomicroscopy, and OCT scans. Following a medical procedure, each quiet was minded at one, three, and a half years. Each visit incorporated an assessment of the accompanying: The BCVA was calculated using IOP and decimal visual acuity. OCT was performed during the one-, three-and six-month follow-up visits.

Data was examined utilizing STATA version 14.2 (Stata et al.: Release 14.2 College Station, TX: Stata Corp LP.). Quantitative information was displayed in terms of mean, standard deviation, median, and range. Qualitative data was supplied in the form of numbers and percentages and compared with the help of either the Chi-square test or the Fisher exact test. P value was deemed significant if it was less than 0.05.

3. Results

A prospective, interventional, comparative study, conducted on 100 eyes of 76 patients with DME, involving two eyes in 24 patients and one eye in 52 patients. 50 eyes received intravitreal injection of aflibercept (IVA group) and other 50 eyes received intravitreal injection of ranibizumab (IVR group). Basic clinical and ophthalmic data demographic data: Table (1); Changes in the BCVA: Table (2); Changes in the CMT: Table (3) and Overall improvement in both groups : Table (4)

Table 1. Distribution of the studied cases according to Basic clinical and ophthalmic data demographic data

VARIABLE	AFLIBERCEPT GROUP N=50	RANIBIZUMAB GROUP N=50	ALL PATIENT N=100	P VALUE
AGE/YEAR				
MEAN ± SD	58.08±7.08	59.28±9.97	58.68±8.63	0.49
GENDER				
FEMALE	13 (35.00%)	14 (36.00%)	27 (36.00%)	0.51
MALE	24 (65.00%)	25 (64.00%)	49 (64.00%)	
EYE				
OD	22 (44.00%)	26 (52.00%)	48 (48.00%)	0.42
OS	28 (56.00%)	24 (48.00%)	52 (52.00%)	
TYPE OF DM				
TYPE 1	2 (5.00%)	1 (3.00%)	3 (4.00%)	1.00
TYPE 2	35 (95.00%)	38 (97.00%)	73 (96.00%)	
DURATION OF DM				
MEAN ± SD	12.04±2.44	11.0±2.11	11.52±2.33	0.02

Table 2. BCVA in decimal at baseline and at follow-up visits in both groups.

VARIABLE	AFLIBERCEPT GROUP N=50	RANIBIZUMAB GROUP N=50	ALL PATIENT N=100	P VALUE
PREOPERATIVE MEAN ± SD	0.13±0.09	0.18±0.06	0.16±0.08	0.0002
POST (1ST MONTH) MEAN ± SD	0.17±0.10	0.21±0.08	0.19±0.09	0.01
POST (3RD MONTH) MEAN ± SD	0.28±0.16	0.29±0.14	0.29±0.15	0.59
POST (6TH MONTH) MEAN ± SD	0.38±0.12	0.28±0.10	0.33±0.12	0.0001
P VALUE FOR REPEATED MEASURE	<0.0001	<0.0001	<0.0001	

Table 3. CMT at baseline and at follow-up visits in both groups

VARIABLE	AFLIBERCEPT GROUP N=50	RANIBIZUMAB GROUP N=50	ALL PATIENT N=100	P VALUE
PREOPERATIVE MEAN ± SD	527.16±141.41 µm	415.88±69.69 µm	471.52±124.21 µm	<0.0001
POST (1ST MONTH) MEAN ± SD	437.36±113.56 µm	371.32±66.92 µm	404.34±98.49 µm	0.002
POST (3RD MONTH) MEAN ± SD	350.48±101.95 µm	331.58±71.48 µm	341.58±88.11 µm	0.48
POST (6TH MONTH) MEAN ± SD	286.9±48.28 µm	351.3±71.68 µm	319.1±68.88 µm	<0.0001
P VALUE FOR REPEATED MEASURE	<0.0001	<0.0001	<0.0001	

Table 4. percentage of improvement in both the groups.

PROGRESSION	AFLIBERCEPT GROUP N=50	RANIBIZUMAB GROUP N=50	ALL PATIENT N=100	P VALUE
IMPROVED	50 (100%)	44 (88.00%)	94 (94.00%)	
STATIONARY	0	4 (8.00%)	4 (4.00%)	
WORSEN	0	2 (4.00%)	2 (2.00%)	0.04

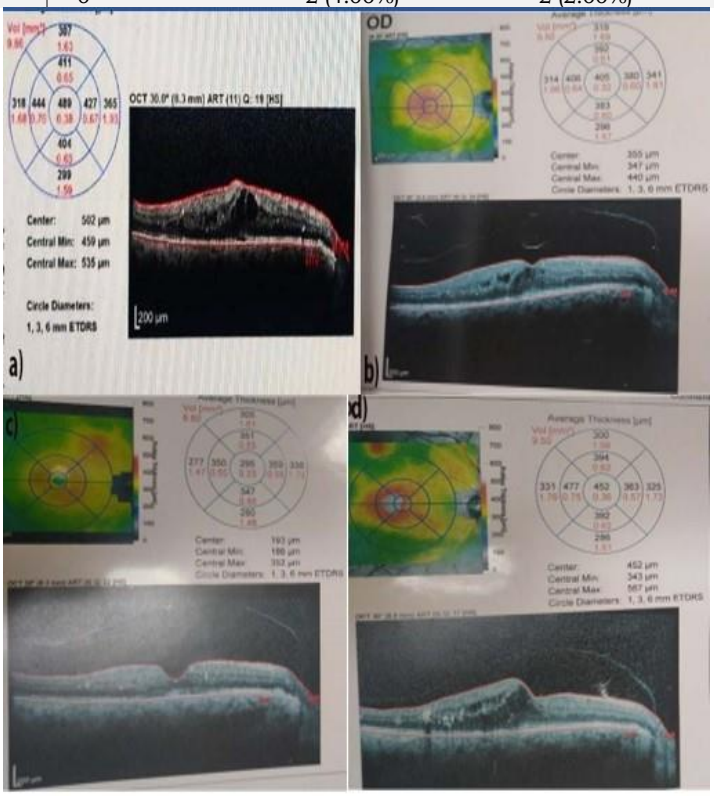

Figure 1. OCT macula of a patient in IVR group at baseline and at 1,3 and 6 months of follow up; (a) OCT before IVR injection (CMT=489u); (b) OCT after 1 months (CMT=405u); (C)OCT after months of IVR

(CMT=295u); (D) OCT after 6 months of IVR (CMT=452u)

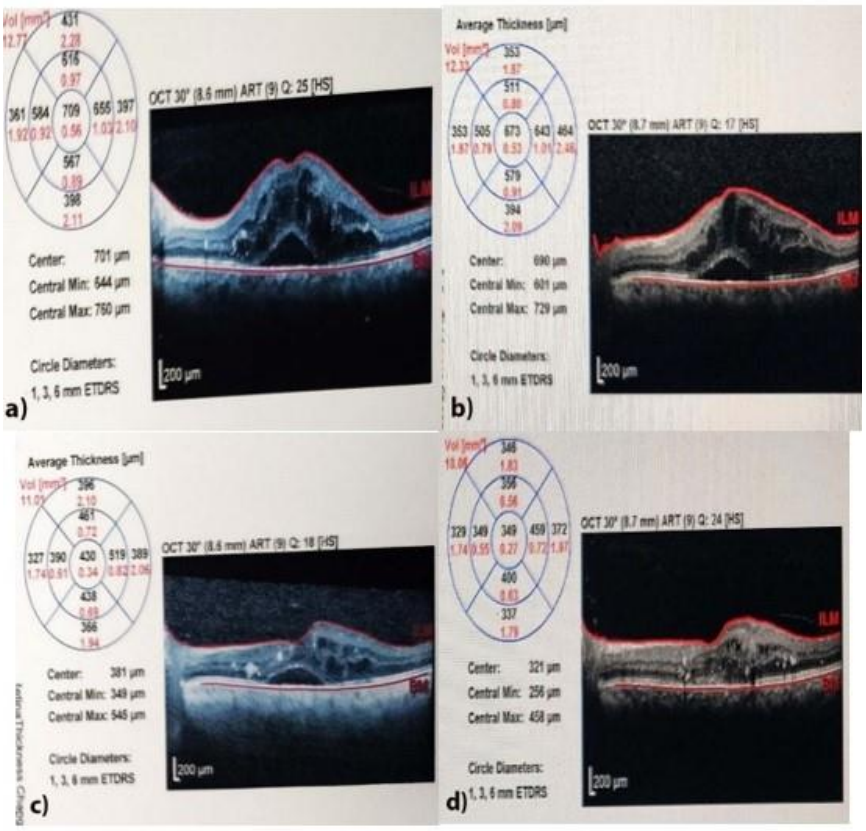

Figure 2. OCT macula of a patient in IVA group at baseline and at 1,3 and 6 months follow up; (A) OCT before IVA(709u); (B) OCT after 1 months of IVA (673u); (c) OCT after 3 months of IVA (CMT=430u); (D) OCT after 6 months of IVA (CMT=349u)

4. Discussion

Today's standard therapy is intravitreal anti-VEGF therapy. Ranibizumab and aflibercept are the two medications that have been authorized for the treatment of DME. They have been demonstrated in a number of studies to be effective in DME. Although VEGF-A is the primary target of both medications, aflibercept also affects VEGF-B and placental growth factor (PGF).[6]

Ranibizumab's binding capacity for VEGF-A165 is roughly 100 times lower than that of aflibercept, predominantly as a result of aflibercept's quicker attachment rates. Aflibercept reduced VEGF-A isoforms' ability to activate VEGFR-1 with 45 to 92 times the potency and VEGFR-2 with 33 to 51 times the potency when compared to ranibizumab.[7]

In order to treat patients with diabetic macular edema, the current study analyses the stability of VA and CMT after intravitreal injections of ranibizumab and aflibercept.

A comparison between the IVA and IVR groups regarding preoperative BCVA revealed a statistically significant decrease in BCVA in the IVA group (P=0.0002). Visual acuity after 1 and 6 months of injection in both groups was compared and showed a statistically significant improvement (P<0.05). However, there was no statistically significant difference between the two groups at the third-month follow-up (p=0.59).

As regards the CMT, the baseline CMT was significantly higher in the IVA group than in the IVR group (<0.0001).

The intergroup comparison of monthly CMT values indicated a marked reduction in CMT in the IVA group over the IVR group, which was statistically significant at the first and sixth-month visits (p=0.002, p<0.0001, respectively). In contrast, at the third-month visit, there was no statistically significant difference between the two groups (P=0.48).

Shimizu et al.[8] in agreement with us, concluded that IVA might be more effective than IVR for enhancing BCVA. This is in line with our findings that the duration of visual improvement in DME patients following consecutive intravitreal injections was significantly longer in the aflibercept group than in the ranibizumab group (6 vs. 3 months).

Despite the fact that both medications improved vision by clearing edema, Meng-Ju Tsai et al.[9] which approves our discoveries, demonstrated that aflibercept actually kept up with vision, with fewer cases of subretinal liquid repeat following a year in certifiable settings.

Shimizu et al.[8] and Meng-Ju Tsai et al.[9], tracked down that the more drawn-out organic movement of intravitreal aflibercept contrasted with intravitreal ranibizumab due to a critical intravitreal VEGF-restricting action of aflibercept, which is roughly multiple times more than ranibizumab, might be the justification for the higher capacity of IVA to keep up with progress in the VA up to the sixth month than IVR. In theory, this will mean that VEGF will be suppressed for 10 to 12 weeks after the injection. Ranibizumab treatment may cause tachyphylaxis or tolerance, according to a number of studies.

According to Wells et al.[10] Patients with diabetic macular edema in the focal point of their vision were helped by intravitreal aflibercept or ranibizumab, but the level of progress differed based on standard visual keenness. There were no tremendous contrasts across research gatherings. Aflibercept was more powerful in further developing vision at lower benchmark visual sharpness values.

Bhandari Sanjeeb et al.[11] demonstrated in a review examination that ranibizumab and aflibercept were both valuable for DME. At a year, they found that the mean changed CST for eyes in the aflibercept bunch was essentially lower than for eyes in the ranibizumab bunch (p 0.01). Moreover, they uncovered that regardless of having somewhat lower benchmark vision and thicker macular tissue, aflibercept-treated eyes showed bigger CST decreases following a year of treatment. More noteworthy VA upgrades were seen after aflibercept treatment, while the starting VA was 20/50 or more terrible.

The findings of Attiat et al.[12] demonstrated that aflibercept may be used to treat DME in eyes that have developed ranibizumab resistance and may be more effective than ranibizumab in treating DME. Additionally, this experiment demonstrated that in patients with lower starting visual acuity values, aflibercept performed better than ranibizumab.

Erden et al.[13] found that both antagonists of VEGFs had similar impacts on visual outcomes. Aflibercept has a speedier and stronger remedial impact on physical results when contrasted with ranibizumab. During the main month visit, visual increase expansions in the IVA group were generally somewhat better, particularly in instances of gentle DME.

On the contrary, Sameh and Ahmed[14] detailed that Aflibercept and ranibizumab are similarly successful at treating DME in eyes with gentle vision misfortune. However, aflibercept requires fewer medication re-infusions and has a lighter treatment load.

This study differed from ours in that it lasted longer (12 m) and included fewer eyes (35 eyes in each group) than ours. It was also noted that the initial VA and CMT showed no statistically significant difference between the two groups, which may explain the difference between these two studies. According to the findings of our study, ranibizumab and aflibercept were both effective; however, aflibercept produced better visual and morphological effects and offered higher stability in CMT after intravitreal injections. Compared to ranibizumab, aflibercept responded substantially more quickly, reducing the central macular thickness and enhancing visual acuity at the site of injection.

Furthermore, in this actual investigation of retrospective observational diabetic macular edema, ranibizumab and aflibercept showed equivalent levels of effectiveness, according to Plaza-Ramos et al.[15] This conflict with our review might have a clarification in the greater review test, which included 213 eyes.

4. Conclusion

Aflibercept and ranibizumab were successful in treating DME. However, Aflibercept produced more stable morphological and visual outcomes. At 90 days after infusion, both aflibercept and ranibizumab had similar outcomes, despite the fact that aflibercept all the more productively safeguarded vision with diminished repeat of macular edema in DME. Rather than people getting ranibizumab, those getting aflibercept experienced a diminished need for extra infusions because of the soundness of their visual additions and enhancements in their focal macular thickness. The useful impacts of aflibercept in patients with starting low visual keenness and expanded macular thickness should likewise be considered.

Disclosure

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