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# Treatment Outcomes of Primary Bevacizumab Injection versus Primary Aflibercept Injection in Diabetic Macular Edema

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## Abstract

**Background:** Visual impairment in diabetic retinopathy (DR) due to diabetic macular edema (DME) is common and disabling for increasing diabetic population all over the world. Varieties of anti-vascular endothelial growth factors (VEGF) had been developed to manage this problem.

**Objective:** To observe and compare the short-term effect of intravitreal Bevacizumab (Avastin) and Aflibercept (Eylea) in patients with DME.

**Methods:** A retrospective cross-sectional study was conducted to assess 40 eyes of 25 patients, 20 eyes received intravitreal Bevacizumab (1.25 mg in 0.05 ml) and the other 20 eyes received intravitreal Aflibercept (2 mg in 0.05 ml) as a line in treatment of diabetic macular edema from January 2022 to February 2024 in Dar-Alsalam Private Eye Hospital in Baghdad – Iraq. A baseline visual acuity (VA) and optical coherence tomography (OCT) were performed in the week prior to the 1st intravitreal injection and were repeated one month after the 3rd intravitreal injection.

**Results:** The study sample involved 40 eyes of 25 patients, 15 of them were males and 10 were females and their ages ranged from 40-77 years (mean age 62.8 years). For Aflibercept group, the VA in log MAR (Mean±SD) showed a highly significant improvement from (0.5±0.39) to (0.31±0.38) after injection. In Bevacizumab group, the mean macular thickness significantly decreased from (458.92±107.1 µm) to (316.0±67.81 µm).

**Conclusion:** Bevacizumab is more effective in decreasing macular thickness while Aflibercept is better in improving VA when treating diabetic macular edema.

**Keywords:** Diabetic retinopathy, diabetic macular edema, Bevacizumab, Aflibercept

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**List of abbreviations:** CMT = Central macular thickness, DME = Diabetic macular edema, OCT = Optical coherence tomography, VEGF = Vascular endothelial growth factor, VA = Visual acuity

## Introduction

Diabetic macular edema (DME) is a major cause of visual impairment in patients with diabetic retinopathy (DR). Impairment of vision will affect quality of life in diabetic adult population [1-5]. The prevalence of diabetes mellitus (DM) is rising worldwide, resulting in an increase in the incidence of DR and DME [6]. Vascular endothelial growth factor (VEGF) has been shown to be a major stimulus in the pathogenesis of DME [7]. Currently the main stay for treating DME are anti VEGF such as Avastin (Bevacizumab) and Aflibercept (Eylea); both drugs targeting VEGF to decrease macular edema but their pharmacological criteria differ that may affect outcomes [8,9]. Bevacizumab is used off-label by ophthalmologist and it is cheaper than

Aflibercept but Aflibercept has longer duration of action than Bevacizumab and U.S. Food and Drug Administration (FDA) approved for ocular condition ([10,11]). Clinical trials have shown that both Aflibercept and Bevacizumab are effective in treating DME, but Aflibercept resulting in more pronounced visual improvement and superior visual outcomes than Avastin. So, the choice between Aflibercept and Bevacizumab will be conditional on factors such as various response to treatment, patient's eye condition, medical history and financial considerations [(11)]. The study objective was to observe and compare the short-term effect of intravitreal Bevacizumab (Avastin) and Aflibercept (Eylea) in patients with DME.

## Methods

A retrospective cross-sectional study was conducted to assess 40 eyes of 25 patients, 20 eyes received intravitreal Bevacizumab (1.25 mg in 0.05 ml) and the other 20 eyes received intravitreal Aflibercept (2 mg in 0.05 ml), each group received three successive injections one month apart as a line in treatment of DME from January 2022 to February 2024 in Dar-Alsalam Private Eye Hospital in Baghdad-Iraq. This is done by reviewing medical records of the patients.

All eyes selected were treated for the 1st time with no previous intervention. One or both eyes from the same patient were selected for this study. Data collected were visual acuity (VA) by algorithm chart and central macular thickness (CMT) by optical coherence tomography (OCT) using Zeiss Angio plex OCT for cirrus HD-OCT 5000. CMT was obtained using the automatically generated thickness map protocol of the OCT device. A baseline VA and OCT were performed in the week prior to the 1st intravitreal injection and were repeated one month after the 3rd intravitreal injection.

The study was approved by hospital ethical review committee.

**Exclusion criteria**

1. Macular edema suspected to originate from other pathologies like central retinal vein occlusion or age-related macular degeneration.
2. The eyes with previously treated DME, whether intravitreal injection or laser therapy.
3. Other associated ocular diseases such as glaucoma.

**Statistical analysis**

In this study, data was double checked and analyzed using IBM SPSS software version 26. Data were expressed as mean and standard deviation in addition to median and range. Wilcoxon and paired Samples t-test were used to compare effect of each drug (Bevacizumab and Aflibercept) on VA and CMT before and after treatment according to normal distribution of data. P value <0.05 was considered as significant and <0.001 as highly significant difference.

## Results

The study sample involved 40 eyes of 25 patients, 15 of them were males and 10 were females and their ages ranged from 40-77 years (mean age 62.8 years). For Bevacizumab group in which 20 eyes received 3 successive intravitreal injection with one month apart, the Mean±SD of VA in log MAR improved significantly from (0.74±0.31) before injection to (0.51±0.34) after 3 injections. While for Aflibercept group in which 20 eyes received 3 successive intravitreal injection with one month apart, the Mean±SD of VA in log MAR highly significantly improved from (0.5±0.39) before injection to (0.31±0.38) after 3 injections (Table 1).

**Table 1. Comparison of visual acuity before and after taking drugs**

| Drug | Measures | VA Before | VA After | P value |
|---|---|---|---|---|
| Bevacizumab | Mean±SD | 0.74±0.31 | 0.51±0.34 | 0.012* |
| | Median (Range) | 0.8 (0-1) | 0.6 (0-0.9) | |
| Aflibercept | Mean±SD | 0.5±0.39 | 0.31±0.38 | <0.001* |
| | Median (Range) | 0.35 (0-1) | 0.15 (0-1) | |

N=20, *P value by Wilcoxon test

Table (2) also shows that in Bevacizumab group, the CMT significantly decreased from (458.92±107.1 µm) before injection to (316.0±67.81 µm) after injection. While in Aflibercept group, the CMT decreased insignificantly from (481.67±101.6 µm) before injection to (381.5±135.19 µm) after injection.

**Table 2. Comparison of central macular thickness before and after taking drugs**

| Drug | Measures | CMT Before | CMT After | P value |
|---|---|---|---|---|
| Bevacizumab | Mean±SD | 458.92±107.1 | 316.0±67.81 | 0.002* |
| | Median (Range) | 444 (343-654) | 300 (250-493) | |
| Aflibercept | Mean±SD | 481.67±101.6 | 381.5±135.19 | 0.211** |
| | Median (Range) | 462 (360-684) | 333 (225-684) | |

N=20, *P value by Wilcoxon test, **P value by unpaired ttest

## Discussion

In this study, Bevacizumab significantly decreases CMT while Aflibercept is better in improving VA.

Aflibercept has been shown to provide better VA outcomes than Bevacizumab by Virgili et al., Hussain and Ciulla and Zhang et al. as well as current study ([8,12,13]).

Wells et al., showed that eyes with VA worse than 20/50 achieved better outcomes in terms of VA and retinal thickness with Aflibercept monotherapy compared to Bevacizumab monotherapy, which is partially agreed with current results regarding significant improvement in VA but not for CMT in Aflibercept regime [(9)].

Jhaveri et al., did not find any evidence of a difference in visual outcomes over two years between treatment with Aflibercept monotherapy and initial treatment with Bevacizumab, while results in this study showed better effect of Aflibercept in outcome regarding VA rather than Bevacizumab [(14)].

In conclusion, Bevacizumab significantly decreases CMT while Aflibercept is better in improving VA when treating DME.

The author recommends to increase sample size with longer duration of follow up in addition to consider other parameters regarding diabetes control like HbA1c.

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## Conflict of interest

The author declares no conflict of interest.

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