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Mini Observational : Changes of Visual Acuity Following Laser
Photocoagulation And Intravitreal
Anti-VEGF Bevacizumab for Diabetic Macular Edema

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CHANGES OF VISUAL ACUITY FOLLOWING LASER PHOTOCOAGULATION AND INTRAVITREAL ANTI-VEGF BEVACIZUMAB FOR DIABETIC MACULAR EDEMA

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ABSTRACT

Introduction: Diabetic macular edema (DME) is the leading cause of vision loss in patients with diabetic retinopathy. Many of current treatment paradigms for managing DME are derived to prevent more severe vision loss and expected to stabilize the visual acuity.

Purpose: To describe the changes of visual acuity after panretinal photocoagulation (PRP) plus intravitreal anti-VEGF bevacizumab injection in treatment of diabetic retinopathy with macular edema.

Methods: A descriptive study was conducted in newly diagnosed patients with severe non proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR) and DME with quantitative measurement of visual acuity before PRP and intravitreal anti-VEGF bevacizumab injection with follow-up visit at least 3 months after treatment.

Results: Total 24 eyes of 19 patients were evaluated. Among this patients, 47,37% were males and 52,63% were females. The mean age was 51 (8,33). Improvement and stabilization of visual acuity was observed. Of the 24 eyes that received PRP plus intravitreal anti-VEGF bevacizumab injection, 7 (29,17%) eyes had stable visual acuity and 10 (41,66%) eyes showed improvement of visual acuity.

Conclusions: PRP with intravitreal anti-VEGF bevacizumab injection as a therapy for patient with diabetic retinopathy and diabetic macular edema was effective to maintain the stability of visual acuity.

Keywords: diabetic retinopathy, diabetic macular edema, panretinal photocoagulation, anti-VEGF bevacizumab

INTRODUCTION

Diabetic retinopathy (DR) is the leading cause of severe vision loss among working-age individuals in developed countries. DR ranked as the fifth most common cause of preventable blindness and fifth most common cause of moderate to severe visual impairment from 1990-2010. The International Diabetes Federation estimates that 285 million individuals worldwide have diabetes mellitus and that approximately 14% of this group

has diabetic macular edema (DME).¹⁻³

DME is the most frequent cause of vision loss in diabetic retinopathy. The treatment of DME has grown rapidly with various approaches to the combination therapy technique that has been developed. The Early Treatment Diabetic Retinopathy Study (ETDRS) group established guidelines for treating patients with clinically significant DME with laser photocoagulation.^{3,4}

Laser photocoagulation can reduce the risk of moderate vision loss by 50%, with 3% of eyes showing vision improvement, (≥ 3 lines) but a substantial proportion of treated eyes remain unresponsive. Panretinal photocoagulation (PRP) has been used to reduce the risk of severe vision loss in severe non proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). These therapy provides a regression of new blood vessels then prevent the progression of DME.^{5,6}

Laser photocoagulation is the mainstay of DME treatment, however the research continues to get more appropriate therapy. A growing body of scientific evidence has implicated vascular endothelial growth factor (VEGF) in the pathophysiologic features of DME. There are 4 major anti-VEGF agents that have been evaluated in treating DME such as pegaptanib, ranibizumab, bevacizumab, and aflibercept. A research study demonstrated the usefulness of an intravitreal injection of bevacizumab, with promising effects in reduction of macular edema, vascular permeability and fibrovascular proliferation in retinal neovascularization secondary to PDR.^{3,5,7}

The purpose of this study is to describe the visual acuity alteration in patient with diabetic retinopathy with macular edema after PRP and intravitreal anti-VEGF bevacizumab injection treatment.

MATERIAL AND METHODS

This was a descriptive study of newly diagnosed, treatment-naïve severe NPDR and PDR patients

conducted at Vitreoretina Unit, Cicendo Eye Hospital National Eye Center between January until June 2019. Patients with diabetes and newly diagnosed DR were enrolled if they met the inclusion criteria.

Inclusion criteria included the following: (1) newly diagnosed severe NPDR or PDR with DME; (2) recieved both of the PRP treatment and intravitreal anti-VEGF bevacizumab injection. Exclusion criteria included the following: (1) other retinal disease than DR; (2) history of prior PRP or intravitreal anti-VEGF injection; (3) inadequate follow-up, defined as missing the 1- and/or 3-month follow-up visits.

Patients baseline characteristic were recorded including age, sex, classification of DR, and baseline uncorrected visual acuity (UCVA). Visual acuity was recorded using Snellen chart. The initial visual acuity is the UCVA before received PRP and anti-VEGF bevacizumab injection, and the final acuity defined as at least 3 months after PRP and intravitreal anti-VEGF injection. The visual acuity said to be stable when same as the initial examination, decrease when visual acuity deteriorates to at least 1 line from the baseline, and increase when there was an improvement at least to 1 line from the baseline. The data retrieved is processed using *Microsoft Excel Office 2013*® software.

RESULT

There were 47 patients newly diagnosed with DR with macular edema who came to the Vitreoretina Unit, Cicendo Eye Hopital National Eye Center between January until June 2019. Total 24 eyes of 19

patients met all the eligibility criteria. Baseline characteristic are shown in Table 1. The mean age (SD) of the patients was 51 (8,33) years and the sex ratio was proportional. 11 (45,83%) patients was diagnosed with severe NPDR and 13 patients (54,17%) with PDR.

Table 1. Characteristics of Patients

Characteristic	Mean \pm SD	N (%)
Sex		
Male		9 (47,37)
Female		10 (52,63)
Age (year)	51 \pm 8,33	
Duration of DM		
< 5 years		9 (47,37)
5 – 10 years		4 (21,05)
> 10 years		6 (31,58)
Classification of DR		
Severe NPDR		11 (45,83)
PDR		13 (54,17)
UCVA		
Baseline		
\leq 3/60		4 (16,66)
4/60-6/18		13 (54,17)
> 6/18		7 (29,17)
Final		
\leq 3/60		6 (25,0)
4/60-6/18		10 (41,67)
> 6/18		8 (33,33)

At the 3-months follow-up visit, the VA of 10 eyes that received PRP and intravitreal anti-VEGF injection improved from the baseline, 7 eyes remained stable, and 7 eyes had worse VA than the baseline as shown in table 2.

Table 2. Final Visual Acuity

Visual Acuity (VA)	PRP + Anti-VEGF (%)
Stable	7 (29,17%)
Improved	10 (41,66%)

Worsened	7 (29,17%)
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DISCUSSION

Diabetic macular edema is an important thing that must be considered in patients with diabetic retinopathy. ETDRS reported that patient with DME have a risk of loss visual acuity. The main goal of the management of the DME is to prevent more severe vision loss.^{1,3,4}

There were 24 eyes of diabetic retinopathy patients with DME who received PRP and intravitreal anti-VEGF bevacizumab injection on January until June 2019 with almost the same sex distribution, with women slightly higher than men. According to Duke Elder, women are more liable to develop diabetes than men (3:2). They are also more likely to develop diabetic retinopathy. Studies have shown that females have a higher risk of developing diabetic retinopathy but proliferation retinopathy is more common in males. The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) stated that there is no difference in prevalence and incidence between men and women.^{8,9}

The most frequent classification of diabetic retinopathy from this study was PDR (54,17%) compared to severe NPDR (45,83%). Similar to the study by Fernando, et al., 56,4% cases were PDR and 25,5% were severe NPDR. Diabetic Retinopathy Study (DRS) showed that the risk of severe visual loss with PDR at the 2-years follow-up examination was 6% in the treated eyes compared with 16% in the untreated eyes.^{7,10}

In this study, 3 months follow-up examination after PRP and

intravitreal anti-VEGF bevacizumab injection showed that there are 10 eyes (41,66%) with improvement of visual acuity. This is accordance with study by Vander et al. which demonstrated increase visual acuity within 3 months of treatment. Kamal, et al., reported improved visual acuity in 10,84% eyes treated with laser and intravitreal anti-VEGF bevacizumab injection compared to patients who only had laser treatment or intravitreal anti-VEGF injection.^{11,12}

There are several factors that influencing clinical outcomes in patient with DME, including age, baseline visual acuity, and the presence of PDR. Chen YP et al. stated that patients with younger age and better baseline visual acuity had better visual outcome and patients with PDR had worse visual outcome after treatment. Channa R, et al., also demonstrated that poor baseline BCVA ($\leq 20/125$) in DME patients predicts poor visual outcome ($\leq 20/100$) after 2 years of treatment with anti-VEGF ranibizumab and/or focal/grid laser, often due to foveal atrophy and/or persistent edema. Similar to that study, the 7 eyes (29,17%) with visual acuity worsened after the treatment because the majority of patients were older age, worse baseline visual acuity and with PDR.^{13,14}

ETDRS reported an increased risk of worsening macular edema leading to loss of visual acuity in patients with pre-existing macular edema at the onset of PRP treatment compared to those without macular edema. There are also limitation and risk to anti-VEGF use. A serious vision-threatening complication of anti-VEGF use in PDR is the development

of tractional retinal detachment (TRD) in the setting of pre-existing membranes. 1 out of 7 eyes with worsening visual acuity caused by TRD.^{15,16}

7 eyes (29,17) had stable visual acuity after PRP and intravitreal anti-VEGF bevacizumab injection treatment. Matheus, et al., also reported the stability of visual acuity of diabetic retinopathy patients with DME after 16 months follow-up examination after PRP and intravitreal anti-VEGF injection. Similar result was reported by Wilczynski M, et al. that the stability of visual acuity after PRP procedure in patients with PDR is 57,81% and 86,11% in patients with severe NPDR.¹⁷⁻¹⁹

A small sample size and short duration of follow-up were limitations of this studies. Systemic conditions related to diabetic retinopathy were not evaluate in this study. Further study included factors influencing the visual and anatomic outcome after PRP and intravitreal anti-VEGF treatment can be conducted with larger sample size and long term follow-up

CONCLUSION

Diabetic macular edema is the most cause of vision loss in patients with diabetic retinopathy. The primary goal of the management of the DME is to prevent more severe vision loss. This study showed that panretinal photocoagulation plus intravitreal anti-VEGF injection treatment is effective in maintaining stability and improvement of visual acuity in patients with diabetic retinopathy with macular edema.

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