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Original Article

The real life data of ranibizumab use among the diabetic macular edema patients in Turkey: Documenting the improvement with clinical optimization during three consecutive years

Abdullah Ozkaya *; Mehmet Ozveren; Ali Demircan

Abstract

Purpose: To report the 12 month real life outcomes of ranibizumab treated diabetic macular edema (DME) patients.
Methods: Treatment naïve DME patients treated with ranibizumab were included. Patients were divided into three groups according to their hospital admittance years (2013, 2014, and 2015) and were compared in regards to the treatment outcomes.
Results: The mean visual acuity change from baseline to month 12 was not statistically significant in 2013 at month 12. The mean BCVA change from baseline to month 12 was statistically better at month 12 in 2014 and 2015. There was a statistically significant difference among the three groups in regards to both mean visit and injection numbers. The mean visit number in 2013 and 2014 were both lower than 2015. The mean injection number in 2013 was lower than both 2014 and 2015.
Conclusions: It is effortful to obey the strict follow-up criteria of prospective studies in DME patients on a PRN regimen. However, optimizing the clinical processes of patient management may lead to improved clinical outcomes in real life.

Keywords: Diabetic macular edema, Intravitreal injection, Ranibizumab

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Introduction

Diabetic macular edema (DME) is the most frequent cause of visual loss among the diabetic retinopathy (DR) patients.[1–5] Different treatment options have been used in the treatment of DME.[2–5] Currently intravitreal injection of anti-vascular endothelial growth factors (Anti-VEGF) and steroids are the most preferred treatment modalities.[3–5] Ranibizumab has been found to be effective with various treatment regimens [i.e. monthly, pro re nata (PRN), treat and extend].[4–9] In pivotal multicenter studies, it was shown that, a mean of 8–9 ranibizumab injections were required in the first year of treatment. However, the mean injection number gradually decreased after the first year throughout the study period.[4–9]

In real life practice, it is not always possible to follow the strict follow-up and retreatment criteria proposed in prospective studies. Pro re nata regimen has been commonly used in Turkey in the treatment of DME.[10] Studies from our country have revealed that the real life practice in regards to the visit and injection numbers was far from ideal.[10–16] Indeed, the mean injection number for ranibizumab was 2.1 during the first 9–12 months of treatment and this is quite low in comparison to the higher injection numbers (up to 7.2) reported from Europe.[10,11]

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Beyoglu Eye Training and Research Hospital, Istanbul, Turkey

* Corresponding author at: Beyoglu Eye Training and Research Hospital, Bereketzade Cami Sok., 34421 Beyoglu, Istanbul, Turkey.
e-mail address: abdozkaya@gmail.com (A. Ozkaya).

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After revisiting our clinical practice in this regard and realizing that monthly visits were not performed regularly for DME patients who were on a PRN treatment regimen, we took some measures after 2013. In this study we aimed to report the 12 months real life outcomes of ranibizumab treated DME patients who were under follow-up in our clinic in 2013, 2014, and 2015, compare the outcomes among the three consecutive years, and summarize the measures taken for improving our visit and injection numbers.

Materials and Methods

Patients

In this retrospective case-control study, medical records of the patients who had DME and underwent intravitreal ranibizumab (IVR) treatment between January 2013 and December 2015 were analyzed. Newly diagnosed treatment naïve DME patients with non-proliferative DR, who completed a follow time of 12 months in our clinic were included. The patients with a history of any other treatment for DME, or showed proliferative DR at admission, or who were lost to follow-up, or received any other treatment for DME including focal or grid laser photocoagulation in the first 12 months during our follow-up were not included. A written informed consent was obtained from all patients before the treatment. The study adhered to the tenets of the Declaration of Helsinki, institutional review board approval was not required for this study according to our countries regulations, as this was a retrospective chart review study.

Data collected from the patients' records included age, gender, best corrected visual acuity (BCVA), central retinal thickness (CRT), and intraocular pressure (IOP) at baseline, and at months 3, 6, 9, and 12. Visit and injection numbers during the first 12 months were also recorded. Patients who admitted in 2013, 2014, and 2015 were grouped and compared in regards to the treatment outcomes, visit, and injection numbers.

Examinations

All patients underwent a standardized examination including measurement of BCVA via a projection chart in decimals at 4 meters, slit-lamp biomicroscopy, measurement of IOP via applanation tonometry, and biomicroscopic fundus examination. Fundus photography, fluorescein angiography (FA) (HRA-2; Heidelberg Engineering, Heidelberg, Germany), and optical coherence tomography (OCT) imaging (Spectralis; Heidelberg Engineering, Heidelberg, Germany) were performed before treatment. All examinations were repeated monthly, except for FA. Fluorescein angiography was repeated according to the physicians' discretion. Optical coherence tomography was used for detecting macular edema and measurement of CRT. Central retinal thickness, defined as the mean thickness of the neurosensory retina in a central 1 mm diameter area, was computed using OCT mapping software generated by the device. Diabetic macular edema was diagnosed via FA and OCT, and patients with a CRT of >300 microns were considered to have DME. The severity of non-proliferative DR, angiographic classification of DME, and ischemic status of macula were not assessed.

Injections

All injections were performed under sterile conditions after application of topical anesthesia, use of 10% povidone-iodine (Betadine; Purdue Pharma, Stamford, CT, USA) scrub was used on the lids and lashes, and 5% povidone-iodine was administered on the conjunctival sac. Intravitreal ranibizumab 0.5 mg/0.05 ml (Lucentis; Novartis, Basel, Switzerland) was injected through the pars plana at 3.5 mm posterior to the limbus with a 30 -gauge needle. Patients were instructed to admit back the hospital if they experienced decreased vision, eye pain, or any new arising symptoms.

Initially, all of the patients received a loading dose of three consecutive monthly injections. Then the patients were followed monthly, and a single injection of IVR was repeated when the VA decreased by one or more lines, or there was an increase of >100 microns in CRT in OCT images compared to the images obtained at the last visit.

Optimization process

In 2013 after reviewing the visit and injections frequency for DME patients in our clinic, we noticed that monthly visits were not performed on a regular basis and injection and follow-up visits were scheduled according to the availability of the calendar. The follow-up and treatment procedures of the DME patients was delayed and it took around 30–50 days to perform the first injection and 100 to 150 days to perform the third injection of the loading phase due to the heavy patient load and scheduling procedures. Therefore, we planned to make some improvements in the clinical processes. Before the optimization process, the DME patients were referred for examination in the retina clinic from the general outpatient and had their appointments in between 1 and 15 days. Similarly, a FA evaluation was performed in between 15 and 20 days, and the first injection was performed in between 15 and 30 days following FA. For those who required monthly follow-up visits, an appointment was scheduled for 40 days later instead of 30 days. As a result, the patient management process was slower than expected and all of the follow-up visits and injections were delayed. After detecting these issues, we planned to make some significant improvements in our clinical practice. Starting from the beginning of 2013, patients referred from the outpatient clinic were consulted and had their FA on the same day in the retina clinic. They received their first intravitreal injection in a maximum of 7–21 days and the next appointment was scheduled for 28 ± 7 later. By achieving these goals, we expected to increase our visit and injection numbers during the first year of treatment in DME patients.

Outcome measures

Primary outcome measure of this study was the change in BCVA and CRT. Secondary outcome measures were the change in CRT and the number of visits and injections.

Statistical analysis

Visual acuity was converted to the logarithm of the minimum angle of resolution (LogMAR) for statistical analysis.

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