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Intravitreal Lucentis (Ranibizumab) as A Treatment for Diffuse Diabetic Macular Edema

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Abstract

Introduction: Humanized anti-VEGF (Vascular endothelial growth factor) antibody fragment Lucentis (Ranibizumab) is prescribed to treat neovascular (wet) age-related macular degeneration, diabetic macular edema, diabetic retinopathy, and myopic choroidal neovascularization. It is also used to treat macular edema following retinal vein occlusion.

Objective: This study was carried out to evaluate the anatomic effect and visual acuity response following intravitreal Lucentis (Ranibizumab).

Methodology: In this investigation, diffuse diabetic macular edema was present in 30 eyes belonging to 30 patients with stable diabetes mellitus. Every eye had undergone argon laser photocoagulation, either Focal, Grid, or pan-retinal

photocoagulation (PRP), for a minimum of three months. The patients with a mean age was 58.13±5.17 years were treated with two intravitreal injections of 0.5 mg of ranibizumab in 0.05 ml spaced four weeks apart. A skilled ophthalmologist assessed each patient's best-corrected visual acuity (BCVA), also assessed their central macular thickness (CMT) using optical coherence tomography, and assessed their diabetic retinopathy at both the baseline and follow-up sessions.

The results: The results showed that the means of BCVA were significantly (P<0.01) decreased from baseline (1.189±0.077 logMAR) to 1 month (0.162±0.058 logMAR) and 3 months (1.109±0.049 logMAR) after injection. Also the results revealed that the mean of CMT were significantly (P<0.01) declined from the baseline (477.47±151.32 µm) to 1 month (438.27±115.68 µm) and 3 month (396.80±115.26 µm) after treatment.

Conclusions: The study concluded that after three months of the second injection of Lucentis (ranibizumab) significantly reduced central macular thickness and improved visual acuity, then diffuse diabetic macular edema is significantly improved and treated using Lucentis (ranibizumab).

Keywords: Lucentis (Ranibizumab), Diabetic, Macular Edema, Vascular Endothelial Growth Factor.

Introduction

Retinal thickening within two-disc diameters of the macula's center is known as macular edema. This condition is caused by alterations in the retina's microvascular structure, which weaken the blood-retinal barrier and allow plasma components to seep into the surrounding retina. Hard exudate rings from microaneurysm leaking are linked to focal edema. Leakage from retinal capillaries, arterioles, and microaneurysms results in diffuse edema.

The most common cause of visual loss in patients with diabetic retinopathy is diabetic macular edema (DME) (1-5). Different treatment approaches have been employed in DME (2-5). The preferred treatment modalities at this moment are intravitreal injection of anti-vascular endothelial growth factors (anti-VEGF) and occasionally steroids (3-5). It has been demonstrated that ranibizumab works well in a variety of DME treatment plans, including monthly, pro re nata (PRN), treat and extend, and others (4-10).

Since 2006, the FDA has approved LUCENTIS (ranibizumab) for the treatment of four severe eye disorders. This approval was granted on February 6, 2015. Patients with diabetic macular edema (DME) and diabetic retinopathy (DR) can now use it (11). In June 2006, LUCENTIS became the first novel molecular entity (NME) to be approved for the treatment of neovascular (wet) age-related macular degeneration (AMD) (12). In addition, it was the first medicine in a brand-new family of drugs that year known as anti-angiogenic ophthalmic agents/VEGF-A (vascular endothelial growth factor) antagonists. In June 2010, after four years, LUCENTIS was granted a second approval for the treatment of macular edema resulting from retinal vein occlusion (RVO) (13). The third indication for ranibizumab was received in August 2012(14-16). Novartis and Genentech, Inc. developed it. Genentech backs use in the United States, whereas Novartis promotes use globally (17).

The best way to understand the pathophysiology of DME is to compare the retina of the eye to film that is placed into the camera, the human eye to a camera that still utilizes film that needs to be developed, and a person's vision to images being shot. In this way, wouldn't you anticipate that a damaged film would result in a damaged picture when it was developed, the same consideration can be made for DME; retinal damage varies in kind, location, and extent, resulting in a vision change that can be either temporary or permanent and range from mild to severe (18).

Blood glucose (BG) irregularities modify the retina's microvasculature, causing the vessel walls to become brittle, leak fluid, and create microaneurysms. These changes make eye issues more noticeable. DME is caused by fluid buildup in the macula, the center region of the retina. Specialized nerve terminals in the macula are responsible for detecting color and are essential for daylight vision. As the injury worsens, hard exudates or retinal thickness cause blurring in the central or lateral vision. Over several months, vision loss worsens and makes it almost impossible to focus. Proliferative diabetic retinopathy (PDR) is the result of decreased oxygen delivery to the retina, which leads to the development of new blood vessels. Although the development of new blood vessels may seem advantageous, this is not the case. This vicious cycle continues because of the instability and ease with which these new capillaries burst (19-21).

Hypertension and fluid retention are the two factors that cause DME and raise the hydrostatic pressure inside the retinal capillaries. The fluid inside these veins is generally stable, but under abnormal circumstances, they exert greater pressures that force fluid out of the capillaries and into the macula, resulting in edema. DME is divided into two groups: diffuse and focal (19-22).

The ideal ranibizumab injection therapy regimen as monthly injection, as-needed, "treat and extend" has not yet been determined. Ranibizumab monotherapy demonstrated a lower progression to proliferative retinopathy than the sham arm, according to the RISE and RIDE study data. This study was carried out to evaluate the anatomic effect as central macular thickness and visual acuity response following intravitreal Lucentis (Ranibizumab).

Material and Methods

The FFA, best corrected visual acuity <0.133, and Hba1C ≤ 7.0% were used to assess diffuse diabetic macular edema in 30 eyes of patients (53.3% females and 46.7% men, Fig. 1.) in this prospective investigation. Those patients suffering from hypertension, chronic renal failure, or uncontrolled diabetes. Individuals patients were subjected recently to laser therapy, other macular or optic disc pathologies were not included (Fig. 2). The age of patients was ranged between 45 to 65 with mean of 58.13±5.17 years.

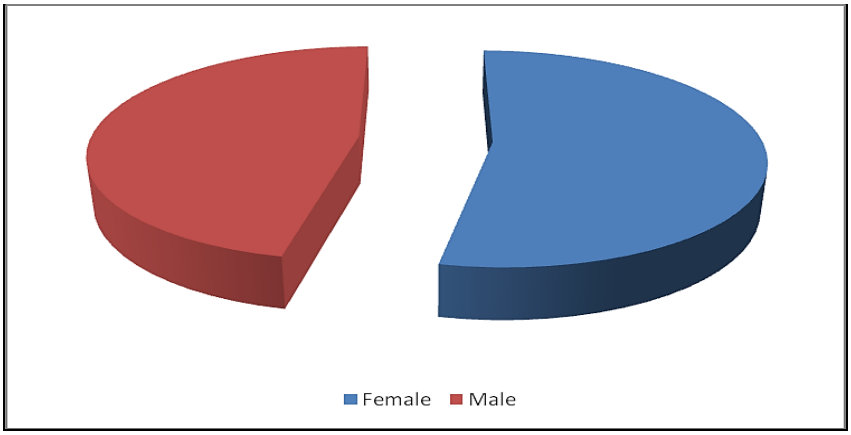

Fig. (1): Patients frequency regarding to gender

Every patient was underwent an ocular evaluation, which included Fluorescein angiography, Best-corrected visual acuity, Bio bio-microscopic anterior segment inspection, and fundus examination using a +90D lens. Optical coherence tomography (OCT) was used to quantify the central macular thickness. One month and three months following the second intravitreal Avastin injection, the study parameters were assessed after the following steps:

- Local anesthetic droplets were applied.
- Lucentis (ranibizumab) was submerged in a sterile environment.

- A 5% aqueous povidone-iodine solution was used to disinfect the eye.
- The eye was held open with a lid speculum.
- Place a swab over the injection site that had been drenched in local anesthetic and hold it there for 60 seconds.
- A measuring caliper was used to establish a secure distance behind the appendix.
- A 30-gauge needle was used to inject 0.5 mg/0.05 cc of ranibizumab, or Lucentis, into the infratemporal quadrant.
- Topical antibiotic was applied.

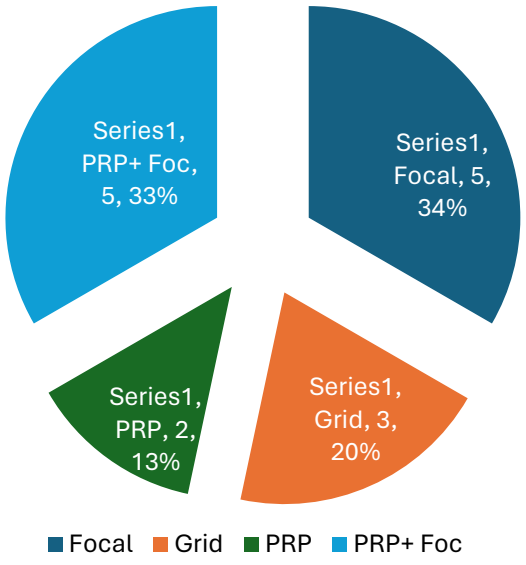

Fig. (2): Percentage of patients who subjected recently to laser therapy

Similar conditions were met for the second injection, which was administered four weeks following the first. Evaluations were conducted on visual acuity, central macular thickness, side effects, and systemic or local consequences.

Statistical Analysis

The collected data such as best-corrected visual acuity (BCVA) and central macular thickness (CTM) at baseline, one month and three months after treatment were analyzed by SPSS software. A paired-samples t-test was applied to compare among the means of baseline, one month and three months. The results were presented as descriptive statistics.

Results and Discussion

If left untreated, diabetic macular edema (DME), a major cause of vision loss in diabetic patients, frequently results in legal blindness. For the different types of DME, popular treatment options include argon laser photocoagulation and intravitreal triamcinolone acetonide. After it was established that vascular endothelial growth factor (VEGF) enhanced retinal neovascularization and increased vascular permeability in diabetic patients, lentils (ranibizumab) were taken into consideration as an additional therapy option for diabetic microvascular endothelial disease (DME).

There was some improvement in the visual acuity of 30 diabetic individuals' eyes with persistent diffuse macular edema. Four weeks apart, each patient had two injections of Lucentis (ranibizumab). Table 1 shows the outcomes at baseline, 1 month and 3 months after the second Lucentis (ranibizumab) injection. The results explained that the mean of best-corrected visual acuity at baseline (BCVA) was 1.189±0.077 **logMAR** and it was significantly ($P<0.01$) greater than that the mean of visual acuity at one months after treatment (0.162±0.058 **logMAR**). Moreover, the results showed that the mean of best-corrected visual acuity at three months after the second intravitreal injection was 1.109±0.049 **logMAR** and significantly ($P<0.01$) lower than that the mean of best-corrected visual acuity at one month after treatment. On the other hand, the results revealed that the mean central macular

thickness (CMT) at baseline was 477.47±151.32 µm and significantly (P<0.01) decreased to 438.27±115.68 µm at first months after injection. Moreover, the CMT was significantly (P<0.01) decreased from one month to end of three months after injection with average 396.80±115.26 µm.

Many authors reported that the various anti-VEGF medications, including pegaptanib sodium, bevacizumab, and ranibizumab, have been used previously in this field (23-24). Therefore a human monoclonal antibody called ranibizumab inhibits every VEGF-A isoform. Similar to present findings was reported by (25) and explained that the intravitreal ranibizumab injection has demonstrated efficacy in treating wet-type age-related macular degeneration in multiple randomized controlled trials. Moreover, many authors (10-12) treated the diabetic macular oedema with ranibizumab and their findings supported the outcome of the present study and they demonstrated that microvascular problems (such as retinopathy) can be delayed or prevented by reducing blood glucose levels to a near normal range. Ranibizumab was examined alongside other VEGF inhibitors, such as pegaptanib, aflibercept, and bevacizumab, in several studies on anti-VEGF medicines for DME that revealed VEGF inhibitors are useful in treating DME (26).

Table (1): Outcomes in 1 month and 3 months (Mean±SD) after the second Lucentis (ranibizumab) injection

Time	Number	BCVA (logMAR)	CMT (µm)
Baseline	30	0.189^{a}±0.077	477.47^{a}±151.32
After 1 month	30	0.162^{b}±0.058	438.27^{b}±115.68
After 3 months	30	0.109^{c}±0.049	396.80^{c}±115.26

BCVA: Best-Corrected Visual Acuity. **CMT**: Central Macular Thickness.
a, b, c: Means with different superscript were significantly different (P<0.0).

In this study, 30 eyes with diffuse diabetic macular edema received an intravitreal injection of Lucentis (ranibizumab), which improved both anatomically and

functionally by reducing the central macular thickness and improving visual acuity. Additionally, there were no instances of clinically significant local or systemic complications during the three-month follow-up period. Generally, the outcomes demonstrate that ranibizumab, or Lucentis, was well tolerated and that no side effects, either systemic or local, were noted during the trial.

Conclusions

Three months following the second injection, Lucentis (ranibizumab) significantly reduced central macular thickness and improved visual acuity. Diffuse diabetic macular edema is significantly improved by using Lucentis (ranibizumab) to block vascular endothelial growth factor (VEGF), which is linked to neovascularization and increased retinal vascular permeability in diabetic retinopathy.

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