Short-Term Intra Ocular Pressure Using Intravitreal *Bevacizumab*

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Abstract: At Ophthalmology Department of Civil Hospital of Culiacán, we investigated the immediate effect of intravitreal injection of *Bevacizumab* on the IOP (intra ocular pressure) 30 min before and 24 h was measured after application of 0.1 mL of *Bevacizumab* (*Avastin*) to 67 patients under sterile technique in operating room, with topical anesthetic tetracaine at 3.5 mm from the sclerocorneal junction. Pre-application average IOP was 13.5 ± 2.6 mmHg, and post-implementation IOP was 13.8 ± 2.6 mmHg. Diagnostics: PDR + MESC (proliferative diabetic retinopathy with macular edema significant clinically) in 26 patients (38.8%), NPDRSC (nonproliferative diabetic retinopathy significant clinical) in 14 patients (20.9%), wet AMD (age related macular degeneration) in 14 patients (20.9%), OCRV (occlusion central retinal vein) in 3 patients (4.5%), OBRV (occlusion of branch retinal vein) in 3 patients (4.5%), SCChR (serous central chorioretinopathy) in 2 patients (4.5%), ChNoA-R (choroidal neovascularization no age related) in 2 patients (3%), CME (cystoid macular edema) in 2 patients (3%).

Key words: *Bevacizumab*, intra ocular pressure, anti-VEGF, PDR, macular edema.

1. Introduction

Angiogenesis is a process that is essential for various physiological processes, such as embryonic and postnatal growth, reproductive functions and the scarring of wounds [1]. Multiple studies in recent decades have established that this process requires a number of steps in endothelial cells and murals where numerous families of ligands involved. However, despite the complexity, VEGF (vascular endothelial growth factor) appears to be necessary for the growth of blood vessels in normal or pathological circumstances [2].

1.1 Antiangiogenic Therapy

The abnormal growth of blood vessels, called

neovascularization, is a central feature of retinal disorders including retinopathy of prematurity, RVO (retinal venous occlusions), proliferative diabetic retinopathy and MDNEA-R (macular degeneration neovascular related to age), which are the leading causes of blindness in both childhood and productive adult life [3]. At present, it is known that inhibiting the angiogenic cascade and vascular permeability effective treatment in ocular neovascularization is achieved as in these pathologies [4]. It is noteworthy that, systemically, it is known that VEGF mRNA (messenger ribonucleic acid) is expressed in a wide variety of human tumors [5]. Then, it is known that this therapy is used successfully to treat different types of cancers such as colon cancer, gastrointestinal, kidney, among others [2].

The introduction of VEGF inhibitors (anti-VEGF) in ophthalmology, represented progress in treating

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many retinal diseases, once deemed untreatable. *Bevacizumab* (*Avastin*) is a murine humanized monoclonal antibody that is directed against all biologically active isoforms of VEGF, there are many studies reporting complications of intravitreal antiangiogenic. One of the reported adverse effects is largely increased intra ocular pressure due to the intravitreal injection.

1.2 Applications in Ophthalmology

1.2.1 Retinopathy of Prematurity

This disease is the number one blind children in Latin America cause. The first major study comparing conventional laser treatment with intravitreal *Bevacizumab* was the BEAT-ROP, in which it was found that monotherapy with *Bevacizumab* (0.625 mg) compared with the laser, in infants with Stage 3+, showed benefits for the Area I, not for Zone II. It also noted that the peripheral retinal vessels continued to grow after treatment, contrary to laser treatment leading to a permanent destruction of the peripheral retina [6].

1.2.2 MDNA-R

The effectiveness of anti-VEGF (*Pegaptanib*, *Ranibizumab* and *Bevacizumab*) agents in terms of stability and improvement in visual acuity after 1~2 years of treatment is known. *Ranibizumab* and *Bevacizumab* have resulted in a comparable improvement together also beneficial visual effects are consistent with the effects on structural changes in the lesion size, in studies fluorangiography and optical coherence tomography [7]. *Bevacizumab* (*Avastin*) is a humanized murine monoclonal antibody produced by DNA (deoxyribonucleic acid) technology from Chinese hamster ovary cells. This antibody is directed against all biologically active isoforms of VEGF, has two binding sites for this factor and to join blocks the effects of VEGF and acts as an antiangiogenic. FDA (Food and Drugs Administration) approved *Bevacizumab* for the treatment of colorectal cancer, because of its low cost compared to other

antiangiogenic, it has been used as an “off-label” since 2004 to treat some retinal diseases [8].

1.2.3 Proliferative Diabetes Retinopathy

There is currently a dose or treatment regimen specific so far [9]. They suggest that anti-VEGF can reduce the risk of intraocular hemorrhage in patients with PDR (proliferative diabetic retinopathy) [10].

2. Materials and Methods

Under informed consent, measurements of intraocular pressure in patients undergoing intravitreal *Bevacizumab*, 30 min before and 24 h after the application were made.

Standardization of measuring instruments for intraocular pressure: Goldman applanation tonometer, Haag-Streit brand. Biomicroscopy: slit lamp; any of the existing models in our Ophthalmology Department. 2.5 mg (0.1 mL) intravitreal injection of *Bevacizumab* was performed under sterile technique in operating room, with topical anesthetic tetracaine 3.5 mm from the corneoscleral limbus; the procedures were performed by medical residents at the service of Ophthalmology at Civil Hospital of Culiacán. We considered high IOP (intra ocular pressure) when exceeded 21 mmHg or when there was a difference equal to or greater than 6 mmHg.

3. Results and Analysis

It was made 98 applications in a total of 67 patients, average age of 65.4 years was obtained (Table 1). Pre-application average IOP was 13.5 ± 2.6 mmHg, and post-implementation IOP was 13.8 ± 2.6 mmHg. There are 98 applications in a total of 67 patients, a total of 35 women, 52.2% representing sample and 32 men, 47.8% being the sample. An average age of 65.4 years was obtained with a standard deviation of 12.9 years, age range 31~89 years no statistical significance ($p = 0.1810$) was found (Fig. 1). Visual acuity was 0.763 ± 0.600 logMAR scale, before application, compared to 0.700 ± 0.589 average ($p = 0.008$) (Fig. 2). The most common vitreoretinal

diseases were: PDR + MESC (proliferative diabetic retinopathy with macular edema significant clinically) at 38.8%, NPDRSC (nonproliferative diabetic retinopathy significant clinical) at 20.9%, macular

degeneration related to age at 20.9% (Fig. 3).

Complications found were subconjunctival hemorrhage in 39 events (39.8%), it increased IOP > 6 mmHg in one patient.

Table 1 Patient's demographics and characteristics.

Characteristics		Frequency (n)	Percentage
Age (mean)		9 ± 12.93	
Injected eye (total 98)	OD	48	48.97%
	OS	50	51.02%
Sex	Female	35	52.2%
	Male	32	47.8%

Fig. 1 IOP (intra ocular pressure).

OD: right eye;

OS: left eye.

Fig. 2 VA (visual acuity).

OD: right eye;

OS: left eye.

Fig. 3 Vitreoretinal diseases distribution.

DME: diabetic macular edema;

AMD: age related macular degeneration;

BVO: Branch retinal vein occlusion;

CSCR: choroidal retinopathy central serous;

CME: cystoid macular edema.

4. Discussion

In our study, we found no significant change in intraocular pressure before and after the application of 2.5 mg (0.1 mL) of intravitreal *Bevacizumab*. This is comparable to the results presented by Güler et al. [11] who analyzed the central thickness of the cornea, the simulated keratometry, the anterior chamber depth, the iridocorneal angle and intraocular pressure in patients who were applied a single dose of 2.5 mg (0.1 mL) of *Bevacizumab*.

5. Conclusions

The use of intravitreal *Bevacizumab* with a 2.5 mg/0.1 mL dose is a choice for patients with any retinal pathology with macular edema. Anti-VEGF therapy is the mainstay for the treatment of many retinal diseases. Despite its promising efficacy in halting the disease and improving the vision for the patients should consider the potential systemic and ocular risks and benefits of receiving intravitreal anti-VEGF therapy and closely monitoring the patients for adverse effects that may occur in the immediate or subsequent periods after administration

of the drugs.

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Conflict of Interest

The authors report no conflicts of interest in this work.

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