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Original Article

Anterior segment changes on ultrasound biomicroscopy after intravitreal anti vascular endothelial growth factor injection

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ABSTRACT

Background: Intravitreal injections are standard of care today and have the potential to change the anatomy of the anterior segment of the eye. This research was undertaken to evaluate the changes in anterior segment anatomy after intravitreal anti vascular endothelial growth factor (anti VEGF) injections.

Methods: We conducted a prospective interventional case series at a quaternary care center where patients undergoing intravitreal injection had pre and post injection ultrasound biomicroscopy (UBM) and intraocular pressure (IOP) measurement after intravitreal anti VEGF injection of 0.05 ml volume.

Results: 75 eyes of 75 patients as per inclusion criteria were studied. A transient rise in IOP post intravitreal injection was found immediately after the injection. The mean rise from baseline was 17 mmHg immediately after injection and IOP returned to normal within 30 min in all cases. Angle measurement done as per established techniques revealed no significant changes in the angles and anterior chamber.

Conclusion: Intravitreal anti VEGF injections had no readily apparent short term concerns. IOP rise was transient and no case was found to have IOP high enough to cause concern for interruption of the optic nerve perfusion or statistically significant narrowing of the anterior chamber angle.

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Introduction

Vascular endothelial growth factor (VEGF) has been implicated in the pathogenesis of age-related macular degeneration (AMD) and other aetiologies of choroidal neovascularisation (CNV). Inhibition of VEGF with various drugs such as Pegaptanib, Ranibizumab and Bevacizumab, is an effective treatment for these and other vascular conditions.[1]

Bevacizumab (Avastin, Roche) is a full-length antibody that has the ability to bind all VEGF isoforms and was developed initially for therapy of colon cancer. Bevacizumab is a humanised recombinant IgG monoclonal antibody that acts by inhibiting VEGF, while Ranibizumab is a humanised monoclonal antibody Fab fragment (IgG1). Ranibizumab (Lucentis, Novartis) has been approved by the US Food and Drug Administration (FDA) for use in AMD.[2] Bevacizumab is also commonly used, although as an off-label treatment for AMD.[3] Both these drugs are in widespread use today and have comparable efficacy.

It is reported that intravitreal injections can cause a rise in intraocular pressure due to the volume of drug injected as well as the specific characteristics of the injected chemical.[4–10] It was our assessment that some of the previously used techniques used to assess the rise in IOP and anterior segment anatomy, in these reports, were not the ideal techniques that could have been used. We aimed to further clarify the effect of intravitreal injection of anti VEGF agents upon intraocular pressure (IOP) and anterior chamber structure using a previously validated technique of Ultrasound biomicroscopy (UBM).[11–13]

Materials and methods

We conducted a prospective study of 79 eyes of 79 patients treated with off-label intravitreal Bevacizumab for various indications. This prospective study had institutional ethics committee approval. Informed consent, particularly in regard to the off-label use and the potential for side effects known to occur with intravitreal administration of Bevacizumab, was obtained from all patients. All patients scheduled to have intravitreal anti VEGF injections for the first time were included provided they consented and had a pre injection ultrasound biomicroscopy (Marvel Ultrasound B scan and UBM, Appasamy, Chennai, India) scan. Patients with distinct history of myocardial infarction or stroke were excluded from the study. Only one eye of any patient was included in the study.

The intravitreal dose of Bevacizumab injected was 1.25 mg/0.05 ml. Bevacizumab was drawn into a 1 ml tuberculin syringe with a 30-gauge needle under complete aseptic precautions in the operation theater. All injections were given by a standard technique wherein, under topical anesthesia, the drug was injected in the inferotemporal quadrant ensuring the visibility of the needle in a dilated pupil. This was followed by an indirect ophthalmoscopy to rule out any bleeding or inadvertent damage and to check optic nerve perfusion. Topical antibiotics were given for 3 days after injection. Intravitreal injection was given 3 mm away from the limbus in pseudophakic eyes and 3.5 mm away from pars plana in phakic eyes. None of our patients was aphakic.

The patients were examined pre- injection in the operation theater where IOP was measured with a Tonopen (Tonopen XL Reichert Technologies, USA). After cleaning and draping, the pre-injection UBM was done using sterile saline. Then, 0.05 ml of intravitreal bevacizumab was given as described. IOP was taken immediately after the procedure after changing the Tonopen sterile cover. Post injection UBM was performed 5 min after the Tonopen measurement, under strict sterile aseptic precautions and a water immersion cup while the patient was still draped. Repeat IOP was measured after 10 min and after 30 min by non contact tonometer. A non contact method was used to minimize using the contact method (Tonopen) multiple times in the immediate post-injection period UBM was repeated after one month to look for any persisting changes in anterior segment parameters.

Measurement of UBM parameters: The following parameters were measured:

1. Central anterior chamber depth (CACD): Measured by drawing a perpendicular line from the center of the cornea at the level of the endothelium and extending till the anterior capsule of the lens. Measurements were read off the calipers on the instrument (Fig. 1).
2. Angle opening distance (AOD): Measured by drawing a 500 μm line parallel to the endothelium starting at the scleral spur and extending toward the central cornea. At the 500 μm point, another line was drawn perpendicular to that point and the distance measured between the corneal endothelium and the point where the perpendicular crossed the peripheral iris (Fig. 2).

Statistical analysis

Data for all patients were entered into a database. Statistical analysis was performed using MS Excel software. Frequency and descriptive statistics were used to analyze the data. The main outcome measurements were intraocular pressure pre and post injection at various time points, for which the repeated measures ANOVA was used. The anterior chamber parameters used were the CACD and peripheral anterior chamber depth as measured by the AOD on UBM.

Results

Baseline characteristics

The mean age ± SD of the patients was 58.88 ± 11.67 yrs, range was 28–80 yrs. Of the patients finally reported, 58 patients were male and 17 were female. 44 right eyes were injected and 31 left eyes were injected. 40 were pseudophakic and 35 were phakic. Pre injection diagnoses were mainly choroidal neovascular membranes, diabetic macular edema or venous occlusion. 79 eyes were initially studied, 4 patients had incomplete data and were excluded from the study leading to a total of 75 eyes.

IOP parameters

Table 1 reports the mean ± std deviation values of IOP at time intervals of 0, 5, 10 and 30 min after intravitreal injection of

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