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ORIGINAL ARTICLE

Effect of Avastin on intraocular pressure before and after intravitreal injections

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Abstract

Introduction: Intravitreal Avastin (bevacizumab) injection is reportedly accompanied by ocular and systemic side-effects. Our enquiry assesses whether there are any differences between intraocular pressure (IOP) in baseline and on the day after injection in patients treated for retinal disease.

Methods: In this experimental study, 82 eyes with retinal diseases that had indication for anti-VEGF and were treated with injections of intravitreal bevacizumab were taken as the case group, and 82 healthy eyes were considered as controls. The IOP was measured by non-contact tonometry in both the healthy eyes and the eyes with retinal diseases before and 24 hours after intervention. Data were analyzed by paired t test and independent t-test in SPSS 19.0 software. Significance level was set at P <0.05.

Results: Results of the study showed that the mean IOP before injection was not significantly different in either groups (p=0.51). However, it was significantly lower after injection than before it in both case and control eyes (p<0.01). The mean IOP changes before and after infusion in the case and control eyes did not differ significantly (p=0.30).

Conclusions: Our study did not find an increased IOP in bevacizumab-treated eyes when compared to fellow control eyes. Further studies with a greater sample size are needed to evaluate whether an increased number of ranibizumab injections is associated with IOP changes.

Key Words: Bevacizumab; Intraocular pressure; Intravitreal Injections

Introduction

Anti-vascular endothelial growth factor (anti-VEGF) antibodies have changed the therapeutic option in ophthalmic diseases such as neovascular age-related macular degeneration (AMD), central vein or branch vein occlusion with macular edema, and diabetic maculopathy (1).

Changes in intraocular pressure (IOP) after repeated intravitreal injections of anti-VEGF have been thoroughly studied since anti-VEGF treatment for exudative AMD was introduced. A transient increase in IOP has been noted after anti-VEGF treatment for exudative AMD; however, it is seldom sustained after a few weeks of observation (2).

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Persistent ocular hypertension (OHT) may occur after intravitreal anti-VEGF injection in patients with no previous diagnosis of glaucoma or OHT. OHT may persist across several visits and patients may require IOP-lowering therapy. Sustained elevation in IOP usually occurs after multiple injections (3).

Methods

In this experimental study, 82 patients with retinal diseases who had indication for Anti-VEGF were incorporated. The protocol of the study was approved by the Institutional Ethics Committee under the identifier IR.BUMS.REC.1394.399. This study measured the intraocular pressure of patients who underwent intravitreal Anti-VEGF due to retinal diseases. Exclusion criteria were preexisting glaucoma, ocular hypertension, uveitis or retina surgery, and history of local or systemic steroid intake. Informed consent was obtained before recruiting the participants in the study. A complete sterile draping and rinsing was performed using topical povidone-iodine under topical anesthesia with anesthocaine 1% eye drops instillation and 1.25 mg Bevacizumab at the lower pars plana with a sharp 30-gauge needle. The injection site was located 3.5 mm posterior to the limbus in pseudophakic eyes and 4.0 mm from the limbus in phakic eyes. They were treated with intravitreal Bevacizumab by a single retina specialist at the retina service of the eye clinic. After intravitreal injection, patients were treated with ciprofloxacin and betamthason eye drops for 3 days. The healthy eyes were considered as controls. The IOP was measured by non-contact tonometry both in the eye with retinal diseases and the healthy eye before and 24 hours after intervention. All additional manipulation was avoided including the subconjunctival injection of anesthetics or application of pressure by forceps. No eye raised intraocular pressure needing IOP-lowering medications or anterior chamber paracentesis before or after intravitreal injection.

Mean IOP pressure and IOP difference before and after intravitreal bevacizuman injections were analyzed by paired t-test and independent t-test in SPSS 19.0 software. Significance level was considered at $P<0.05$.

Results

The result of the study showed that 41 (50%) of the patients were male and 41 (50%) were female. From 82 eyes with retinal diseases, 43 eyes (52.4%) were on the right and 39 eyes (47.6%) were on the left. Forty-one eyes (59%) had single injection, 39 eyes (41%) had repeated injections.

Range of IOP in intervention eyes was 10 to 22 mmHg and in control eyes 10 to 23. Independent t-test results showed that the mean IOP was not significantly different in case or control eyes before and after injection ($p=0.51$). However, paired t test showed that after injection, it was significantly lower than before in both the case and control groups ($p<0.01$). The mean IOP changes before and after infusion in the treatment and control eyes did not differ significantly ($p=0.30$)(Table 1).

Table 1: Comparing IOP means before and after injection in case and control eyes

Group	Before	After	P-Value	Difference before and after intervention
	Mean±SD	Mean±SD		Mean±SD
Case	14.12±2.95	13.13±3.08	0.002	2.85±0.99
Control	14.29±3.23	12.96±2.84	<0.001	2.57±1.33
P-Value	0.51	0.51		0.30

Discussion

This study did not find any significant difference in terms of intraocular pressure before and 24 hours after Bevacizumab intravitreal injection. None of the 82 patients had elevation of IOP more than 21 mmHg after 24 hours of injection of intravitreal Bevacizumab. The mean IOP at baseline was 14.12±2.95; on the day after injection, it was 13.13±3.08 mmHg in the case eyes and 12.96±2.84 in the control eyes. Our results confirmed several other studies that detected no correlations between anti-VEGF injections and delayed IOP elevation overall.

The incidence of sustained elevated IOP in patients receiving intravitreal anti-VEGF injection is significant. Additionally, these data suggest the possibility of a heightened risk for further elevation of IOP in patients with pre-existing glaucoma who receive either bevacizumab or ranibizumab. Prospective studies are needed to verify these results and better understand the implications of this finding (4,5).

Alice LY and colleagues described that until now, few studies have described a sustained IOP elevation after anti-VEGF injection. They found an increased risk of IOP elevation in patients receiving≥29 injections compared to patients with ≤12 injections (1). Nevertheless, our data could not confirm that there is an increased IOP for patients with multiple injections that could be due to the

lower number of injections in our study in comparison to this report.

Intravitreal injection of bevacizumab is safe with respect to short-term IOP changes, as almost all IOPs returned to a safe range (<25 mmHg) within 30 minutes. Elevated IOP 30 minutes after injection only occurs rarely, so routine prophylactic use of anti-glaucoma medication is not indicated (6). Eye massage by cotton swabs after intravitreal injection produces a significantly lower IOP spike after the injection (7). In this regard, IOP return to normal range can be attributed to this parameter in our study.

There are several hypotheses for the potential mechanisms underlying an IOP increase after anti-VEGF injections. It is assumed that Bevacizumab may block the trabecular meshwork or Schlemm's canal by an unknown mechanism, inflammatory mechanism or an immunological reaction or a traumatic mechanism (1).

Conclusions

In summary, we could not detect any association between the injections of intravitreal Bevacizumab and the level of IOP in patients in spite of multiple injections. Based on our results, we cannot claim a compelling necessity for postoperative IOP controls after injections of intravitreal bevacizumab. However, with increasing age of the patients, the chance of increasing intraocular pressure raises too. Therefore, regular IOP control is recommended as a trend toward IOP elevation.

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Conflict of interest

The authors declare no conflict of interest.

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