Original Article

Evaluation of intraocular pressure change and anterior segment parameters after intravitreal bevacizumab injection – Cannula size matters

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Abstract:

PURPOSE: To determine the changes in intraocular pressure (IOP) and anterior chamber parameters following intravitreal bevacizumab injection with different sizes of cannulas.

METHODS: This clinical trial was conducted with 70 eyes of 70 patients who received an intravitreal injection of bevacizumab with 26 G (Group 1) or 30 G (Group 2) needle. Preinjection and postinjection 30th-min IOP and pentacam measurements were obtained. Anterior chamber depth (ACD), anterior chamber volume (ACV), central corneal thickness (CCT), corneal volume (CV), and iridocorneal angle (ICA) measurements were evaluated in pentacam.

RESULTS: Preinjection mean IOP values in Group 1 and 2 were 14.7 ± 3.29 mm Hg and 15.1 ± 2.87 mm Hg, respectively. Postinjection mean IOP in Group 1 was 16.8 ± 6.24 mm Hg and in Group 2 was 20.3 ± 3.66 mm Hg. Postinjection mean IOP values were significantly higher than preinjection values in both groups (Group 1 $P < 0.005$ and Group 2 $P < 0.001$). IOP change was significantly higher in Group 2 after injection ($P < 0.05$). In both groups, the change in IOP found to be more significant in phakic eyes than pseudophakic eyes (Group 1 $P < 0.001$, Group 2 $P < 0.001$). CCT and CV were significantly higher in both groups 30 min after the injection than preinjection (Group 1 and Group 2; $P < 0.01$). In Group 2 ACD, ACV and ICA values were significantly lower than preinjection values ($P < 0.05$).

CONCLUSION: Needle bore size is an important parameter that influences anterior segment parameters and IOP change in the intravitreal injection. IOP rise and anterior segment changes are more prominent with a thinner cannula.

Keywords:

Bevacizumab, intraocular pressure, intravitreal injection, pentacam

Introduction

Intravitreal injections are applied in the treatment of a variety of retinal diseases. Inflammatory and edematous sequelae of certain diseases such as choroidal neovascularization, diabetic macular edema, and retinal vascular occlusion are a prime indication for their use. The most expanding indication today for intravitreal injections is exudative age-related macular degeneration in which most patients require repeated injections. Anti-vascular endothelial growth factors (anti-VEGF) such as bevacizumab, ranibizumab, and aflibercept are commonly used agents in intravitreal injections. The most important complications of intravitreal injections are endophthalmitis, crystalline lens and capsule damage, imminent and sustained intraocular pressure (IOP) rise, intravitreal hemorrhages, and peripheral retinal tears. After intravitreal injections, IOP may rise up to 70–80 mmHg in 5 min, and it decreases back to normal values after 30th min with most agents.[1,2] Even in anti-VEGF injections sustained IOP rise can be seen up to 6% of the cases. Risk factors

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were glaucoma history, high IOP before injection, and lens status (more risk in phakic eyes).[3] Long-lasting pressure rise can cause permanent optic disc damage and retinal nerve fiber loss. It is known that the cannula size may be an essential factor in contributing increased IOP during injection. However, it has never been studied prospectively among patient undergoing intravitreal injection. In this project, we aimed to demonstrate the impact of cannula size on IOP and anterior segment parameters.

Methods

Seventy eyes of 70 patients who received 0, 1 ml intravitreal bevacizumab in ophthalmology outpatient clinic at Uludag University School of Medicine between September 2012 and October 2012 were included. Participants were divided into two groups according to cannula size: 26 G cannula (Group 1) and 30 G cannula size (Group 2). Indications for injections were age-related choroidal neovascularization, retinal vascular occlusions, diabetic retinopathy, and diabetic macular edema. The exclusion criteria included preexisting glaucoma, past vitreoretinal surgery, uveitis, high myopia (>−5.0 D), and high hyperopia (>+5.0D). The Institutional Review Board/Ethics Committee of Uludag University approved the study protocol. All procedures conformed to the tenets of the Declaration of Helsinki for research involving human participants.

Patients signed an informed consent form which described the potential risks and benefits of the procedure and follow-up management, IOP measurements, and Pentacam imaging. Injections were administered in clean room conditions by the standard clinical protocol at our clinic.

Approximately 30 min before injection both pupils were dilated through cyclopentolate 1%. Following topical anesthesia with proparacaine, 5% povidone-iodine was applied to the ocular surface to provide antisepsis. In the supine position, periocular antisepsis was achieved by 10% povidone-iodine and while fixating eye with cotton tip applicator, 0.1 ml of intravitreal bevacizumab injection performed in the upper temporal region with a distance of 3.5 mm to the limbus without the scleral tunnel. After injection, cotton tip applicator was pressed on application site for about 30 s to avoid reflux and subconjunctival hemorrhage. To minimize the risk of endophthalmitis, physician put a mask on during the whole procedure. During the procedure, none of the patients needed urgent paracentesis. All of the participants used fluoroquinolone eye drops for 5 days to avoid postprocedure infection.

Thirty minutes before and after intravitreal injection IOP of all the participants was measured by the same physician using Goldmann applanation tonometer. Pentacam (Oculus, Wetzlar, Germany) measurements were also taken 30 min before and after injection. Pentacam imaging was performed with the patient seated, using a chinrest and forehead strap. Before each measurement one drop of lubricating eye fluid was instilled. Central corneal thickness (CCT), corneal volume (CV), anterior chamber depth (ACD), anterior chamber volume (ACV), iridocorneal angle (ICA), and anterior/posterior corneal curvature values were noted.

Statistical analyses were performed using the SPSS software for Windows version 17.0 (SPSS, Inc. Chicago, IL, USA). Distribution analysis was performed by the Shapiro–Wilk test. *t*-test was used in normal distributed data groups comparison and Mann-Whitney U-test was used in abnormally distributed data group comparison. For dependent group analysis, Wilcoxon signed rank test was used. The Pearson Chi-square and Fisher's exact test were the tests of choice in categorical data survey. $P = 0.05$ was accepted as statistically significant in 95% confidence interval.

Results

Of the 70 patients enrolled, 43 (61%) were male and 27 (39%) were female. Intravitreal injection was performed using 26 (Group 1) and 30 (Group 2) gauge cannula in 37 (53%) and 33 (47%) patients, respectively. The mean age in Group 1 was 67.4 ± 11.4 years and in Group 2 was 71.3 ± 9.9 years.

Indications for intravitreal injection are shown in Table 1. In Group 1, 38% of participants were phakic and 62% were pseudophakic. In Group 2, 45% were phakic and 55% of them were pseudophakic. Groups were identical regarding lens status and indication of injection ($P > 0.05$). The differences between the groups regarding age and preinjection values of CCT, CV, ACD, and ICA were not significant ($P > 0.05$). The mean preinjection ACV value was higher in Group 1 than in Group 2 ($P < 0.01$).

Preinjection mean IOP values in Group 1 was 14.7 ± 3.29 mmHg and in Group 2 was 15.1 ± 2.87 mmHg ($P < 0.05$). Postinjection mean IOP in Group 1 and Group 2 was 16.8 ± 6.24 mm Hg and 20.3 ± 3.66 mm Hg, respectively. Postinjection mean IOP values were significantly higher than preinjection in both groups (Group 1 $P < 0.05$ and Group 2 $P < 0.001$). IOP change after injection was greater in Group 2 than in Group 1 ($P < 0.05$). Mean IOP changes in the pseudophakic and phakic eyes were 1.6 ± 0.7 mm Hg and 2.5 ± 1.2 mm Hg in Group 1, respectively, 4.5 ± 1.8 mm Hg and 5.9 ± 1.3 mm Hg in Group 2, respectively. In both groups, the change in IOP found to be more in phakic eyes than in pseudophakic eyes (Group 1 $P < 0.001$, Group 2 $P < 0.001$).

The mean CCT, CV, ACD, ACV, and ICA values before and after injection are shown in Table 2. CCT and CV were significantly higher in both groups 30 min after the injection than preinjection ($P < 0.01$). In Group 1, ACD, ACV, and ICA values did not change after injection ($P > 0.05$). Postinjection ACD, ACV, and ICA values were significantly lower than preinjection values in Group 2 ($P < 0.05$).

Discussion

For the first time in 1945, intravitreal injections were used in the treatment of intraocular infections after the intravitreal application of crystallized penicillin in experimental

staphylococcal endophthalmitis.[4,5] Subsequent intravitreal gas injections were included in the treatment of retinal tears. However, rapidly increasing the number of intravitreal applications coincides with times that the effect of intravitreal triamcinolone on retinal neovascularization was noticed.[6] With this rapid acceleration, intravitreal injections with their complications take place in ophthalmology practice. The most important complications of intravitreal injections include endophthalmitis, early IOP elevation, crystalline lens trauma and associated cataracts, intra-vitreous hemorrhages, and retinal tears. Complications and ways to prevent them have become an important field of the study. In order to minimize the complications, many authors attempted to define appropriate injection techniques.[7-9]

One of the most significant complications of intravitreal injection is early sudden IOP elevation. Similarly to our study, Soheilian *et al*.[10] measured mean IOP changes of 6.5 ± 6.3 mm hg at 30 min after intravitreal bevacizumab injection using a 30 g needle. Permanent elevation of IOP due to increased recurrent injections has been reported extensively.[11-13] In 2007, Hollands *et al*.[14] performed a study of 107 patients and reported that the IOP of three patients could not be relieved after injection. They demonstrated that IOP was higher in phakic patients than in pseudophakic patients. Similarly, in our study, we also showed that the IOP change in phakic patients was higher in both groups than the pseudophakic patients.

Kim *et al*. published a study of early IOP changes after intravitreal bevacizumab with 213 patients and showed that the small cannula size used for intravitreal injection was significantly associated with high IOPs.[15] In 2010 Lorenz *et al*.[16] graded patients with intravitreal anti-VEGF according to paracentesis needs and subconjunctival reflux quantities to evaluate the effect of cannula diameter on IOP rise using 27G and 30G cannulas. Reflux in the study was evaluated based on observation. Subconjunctival reflux was less in patients with thinner cannulas and requiring paracentesis more frequently due to increased early IOP. In our study, we compared IOP and anterior segment parameters 30 min before and after bevacizumab injection with two different sizes of cannula. In previous studies, it was concluded that IOP resolves to relatively normal values after 30 min. Hence, the measurements were delayed to observe the prolonged changes. In order not to increase infection risk, IOP measurements were limited to the single time period. In thinner cannula group, IOP rise was significantly more than the large cannula group. However, since early IOP values were not measured, it was not possible for us to evaluate the effect of reflux. The amount of reflux has not been investigated since it is not an objective method.

Early anterior segment parameter changes after intravitreal injection were studied by Kerimoglu *et al*.[17] to assess the effect of lens status. In this study, triamcinolone acetonide was used for injection. Following intravitreal injection of 0.1 ml triamcinolone acetonide, without vitreous reflux, IOP decreased to safe levels more quickly in pseudophakic eyes than in phakic eyes. The study was not interested in the effect of cannula diameter. In our study in both groups, the change in IOP found to be more in phakic eyes than in pseudophakic eyes.

Arslan *et al*.[18] showed that ACD was significantly lower 1 month after the first and second anti-VEGF injections than at the level of preinjection.

In our study, ACD and ACV decreased in both groups at 30 min postinjection compared to preinjection values. However, this change was statistically significant only in the group with thinner cannulas. Although the IOP value decreased to 30 mmHg at 30 min, it was observed that the reduction in ICA with ACV and depth continued to be significant in patients using thinner cannulas. CCT and CV were significantly higher in both groups than preinjection values. There was no significant difference between groups regarding CCT and CV. This change was thought to be corneal edema associated with povidone-iodine and proparacaine used during the procedure in both groups.

Our analysis lacked the data on the number of previous injections and time passed over the last injection. It is known that the increase in the number of injections is a predisposing factor for higher IOP values. The axial lengths of the patients were unknown. All patients received a standard injection of a drug (0.1 ml). However, globe volume is an effective parameter on IOP change. Further studies needed to evaluate this parameter and make the injection amount accordingly.

Table 1: Intravitreal injection indications

	CNV	DRP	RVO	RAP	Total
Group 1, *n* (%)	15 (36.5)	11 (29.7)	8 (21.6)	3 (8.1)	37 (100)
Group 2, *n* (%)	16 (48.4)	12 (36.3)	5 (15.3)	-	33 (100)
Total, *n* (%)	31 (44.2)	23 (32.8)	13 (18.6)	3 (4.2)	70 (100)

CNV=Choroidal neovascularization; DRP=Diabetic retinopathy; RVO=Retinal vascular occlusion; RAP=Retinal angiomatous proliferation

Table 2: Mean values of anterior chamber parameters before and after injection

	26 Ga (Group 1)			30 Ga (Group 2)		
	Preinjection	Postinjection	*P*	Preinjection	Postinjection	*P*
CCT (nm)	553.21±38.7	585.35±40.1	<0.01	554.6±34.3	591.2±34.5	<0.01
CV (mm³)	58.94±4.0	61.66±4.0	<0.01	59.54±4.8	62.66±4.6	<0.01
ACD (mm)	2.99±0.9	2.97±0.9	>0.05	2.77±0.6	2.60±0.7	<0.01
ACV (mm³)	164.02±48	162.1±43	>0.05	150.02±32.3	147.84±32	<0.01
ICA (°)	33.31±9.8	34.3±11	>0.05	33.96±9.3	34.01±9.2	<0.05

CCT=Central corneal thickness; CV=Corneal volume; ACD=Anterior chamber depth; ACV=Anterior chamber volume; ICA=Irıdocorneal angle

Conclusions

We demonstrated that intravitreal injections with thinner cannulas and in phakic eyes have a higher risk for IOP rise that reflects ACD and ACV. So that, phakic patients using thinner cannula for injection should be monitored more closely after intraocular injections. However, further studies are required to understand risk factors for sustained IOP rise such as axial length and number of injections.

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Conflicts of interest

There are no conflicts of interest.

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