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ORIGINAL ARTICLE

Long – Term Intraocular Pressure Changes after Intravitreal Injections

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Summary
Introduction. Direct drug delivery by intravitreal injection is an essential tool in the treatment of retinal diseases and the studies have demonstrated that patients undergoing treatment with intravitreal anti-VEGF agents may experience sustained and delayed elevation of intraocular pressure. According to literature, the incidence of sustained elevation of intraocular pressure varied from 3.45% - 11.6%.
Aim of the Study. To research the changes of intraocular pressure after intravitreal injections in patients with a diagnosis of age-related macular degeneration, diabetic maculopathy, and retinal vein occlusions.
Material and Methods. A prospective study was done in Pauls Stradins Clinical University Hospital, Riga, Latvia from November 2015 – January 2016. In this study were interviewed and examined 31 patients who had had intravitreal injections. For data analysis, SPSS 23 was used.
Results. From 31 patient there were 20 (65.5%) females and 11 (35.5%) males. They were divided into three groups depending on the diagnosis. There were 26 (83.9%) patients with age-related macular degeneration, 3 (9.7%) with diabetic retinopathy and 2 (6.5%) with retinal vein thrombosis. From 31 patient the IOP after intravitreal injections were increased in 21 (67.7%) patient - 13 (41.9%) in the right eye and 10 (32.2%) in the left eye. In both eyes the pressure was increased from 14 to 17 mmHg (14.08 to 17.08 mmHg in the right eye and 14.1 to 17.3 in the left eye). From 6 (19.3%) patients who had glaucoma before intravitreal injections, in 4 (66%) intraocular pressure had increased from 14.7 to 18.5 mmHg in the right eye and from 12.5 to 17 mmHg in the left eye.
Conclusions. Patients with previously diagnosed glaucoma had a greater rise in intraocular pressure compared to patients with no glaucoma diagnosis. Further studies with a greater number of patients and identical intraocular pressure measuring method before and after injections are needed to better evaluate the effects of intravitreal injections on intraocular pressure.
Key words: intravitreal injections, intraocular pressure, age-related macular degeneration

INTRODUCTION

Direct drug delivery by intravitreal injection is an essential tool and has become the method of choice in the treatment of retinal diseases, such as age-related macular edema, diabetic retinopathy and retinal vein occlusion. Although intravitreal injection is a rather safe method of treatment and the risk of serious vision-threatening complications is quite low (0.019-0.06%) (8,11), studies have demonstrated that patients undergoing treatment with intravitreal anti-VEGF (Anti-vascular endothelial growth factor therapy) agents may experience not only acute, but also sustained and delayed elevation of intraocular pressure , which is significantly important to patients with glaucoma. As studies have shown, patients with pre-existing glaucoma have higher rates of intraocular pressure intraocular pressure after injection compared to patients with no glaucoma (4). According to literature, the incidence of sustained elevation of intraocular pressure varied from 3,45%-11,6% (3).

AIM OF THE STUDY

In this prospective study intraocular pressure changes were analyzed 2 - 18 weeks after injection of ranibizumab or bevacizumab. The aim of this study was to research the changes of intraocular pressure after intravitreal injections in patients with a diagnosis of age-related macular edema, diabetic retinopathy or retinal vein occlusion and also to compare the rise of intraocular pressure in patients with and without pre-existing glaucoma diagnosis.

MATERIAL AND METHODS

In this prospective study was interviewed 31 patient and examined 40 eyes of 31 patient who had been treated with intravitreal injections of ranibizumab or bevacizumab. The prospective study was done in Pauls Stradins Clinical University Hospital from November 2015 – January 2016. In this study were interviewed and examined 31 patients who had had intravitreal injections.
The study included demographics and clinical course. The examination included visual acuity, intraocular pressure measurement by Icare, slit lamp examination and fundus exam. The intraocular pressure was measured 2-18 weeks after injection and compared to measurements made before the first injection of the anti-VEGF agent. The minimum follow-up period was 2 weeks. Ocular hypertension was defined as intraocular pressure above 21 mmHg.
From 31 patient there were 20 (65.5%) females and 11 (35.5%) males. The mean age of patients was 76.13 ± 13.36. They were divided into three groups depending on the diagnosis. There were 26 (83.9%) patients

with age-related macular degeneration, 3 (9.7%) with diabetic retinopathy and 2 (6.5%) with retinal vein thrombosis. In this study was also compared the rise intraocular pressure in patients with and without pre-existing glaucoma. For data analysis SPSS 23 was used.

RESULTS

From 31 patient the intraocular pressure after intravitreal injections was increased in 21 (67.7%) patient. The average increase was from 14.1 to 17.2 mmHg. In both eyes the pressure was increased from 14 to 17 mmHg (14.08 to 17.08 mmHg in the right eye and 14.1 to 17.3 in the left eye). From 6 (19.3%) patients who had glaucoma before intravitreal injections, in 4 (66%) intraocular pressure had increased from 14.7 to 18.5 mmHg in the right eye and from 12.5 to 17 mmHg in the left eye. From 6 patients with pre-existing glaucoma diagnosis, 4 (66%) had an increase of intraocular pressure, average 14 to 18 mmHg.

There were two patients, who had a significant rise of intraocular pressure. Patient 1 developed intraocular hypertension: An 84-year-old Caucasian female was treated for age-related macular degeneration OU. She had intraocular pressure asymmetry before starting injections - intraocular pressure OD was 11 mmHg and OS was 18 mmHg. At the time of measurement, the IOP was still asymmetric and there was intraocular hypertension in OS – intraocular pressure OD was 8 mmHg and intraocular pressure OS was 22 mmHg. The number of injections was 6 in OD and 9 in OS. The patient didn't have pre-existing glaucoma diagnosis.

Patient 2: Also an 84-year-old Caucasian female was treated for age-related macular degeneration OS. She had 3 injections and intraocular pressure increased significantly - from 18 to 21 mmHg. The patient didn't have pre-existing glaucoma diagnosis.

The mean number of injections in the right eye was 7.6 (in a range from 3 to 40) and in the left eye 6.3 (in a range from 3 to 24). There was no statistically significant correlation between injection number and the rise of intraocular pressure (p=0.449). There was also no correlation between the rise of intraocular pressure and the diagnosis, that anti-VEGF agent was used for.

DISCUSSION

Persistent rise of intraocular pressure following intravitreal anti-VEGF agents is a recently reported condition. There are several large studies, that examined the efficacy of Lucentis (ranibizumab) injections in neovascular age-related macular degeneration – MARINA and ANCHOR trials. These studies included hundreds of patients who received intravitreal injections of Lucentis at four-week intervals. A post hoc analysis was done and intraocular pressure had raised at least 6 mmHg compared to intraocular pressure before initiation of treatment (10). In ANCHOR study intraocular pressure elevations were found in 3.6% of treated eyes, compared to 0% in the control group (1).

The cause of such protracted intraocular pressure elevation is not completely understood. Several mechanisms have been suggested, including trabecular damage caused by repeated intraocular pressure elevations following each injection, a direct toxic effect of the medication on trabeculum, trabeculitis caused by compounds injected, disrupted drainage of the aqueous humor by proteins of silicone particles, which can be found in syringes used for the intravitreal injection that penetrate the trabeculum (5,7), damage to the drainage system caused by repeated intraocular pressure elevations immediately postinjection, and mechanical injury to the drainage sytem (9).

Another considerable cause of sustained elevation of intraocular pressure is glaucoma. Patients with pre-existing glaucoma diagnosis should be monitored closely during treatment with intravitreal injections, and glaucoma therapy should be increased if needed. The ophthalmologist can also consider tapping anterior chamber before injection by making a paracentesis to decrease the pressure in the eye before doing the injection. That minimizes the volume effect when the drug is injected.

CONCLUSIONS

Anti-VEGF therapy is the mainstay for the treatment of many retinal diseases, (6) but recent studies have shown, that multiple anti-VEGF injections may lead to an increase in intraocular pressure, although this variation is not sufficient to cause the development of ocular hypertension in the majority of patients (2). In this study a greater number of intravitreal injections is not associated with an increased risk of intraocular pressure. Patients with previously diagnosed glaucoma had a greater rise in intraocular pressure compared to patients with no previous glaucoma diagnosis. Further studies with a greater number of patients and identical intraocular pressure measuring method before and after injections are needed to better evaluate the long-term effects of intravitreal injections on intraocular pressure.

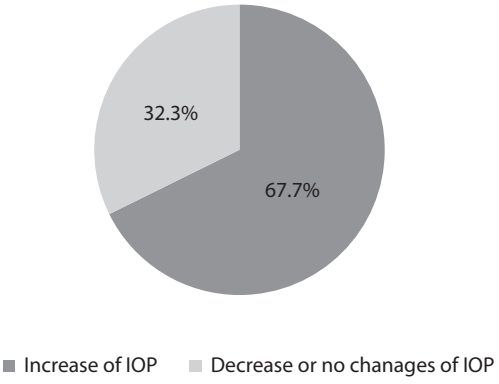

Fig. 1. Changes of intraocular pressure (IOP) in patients

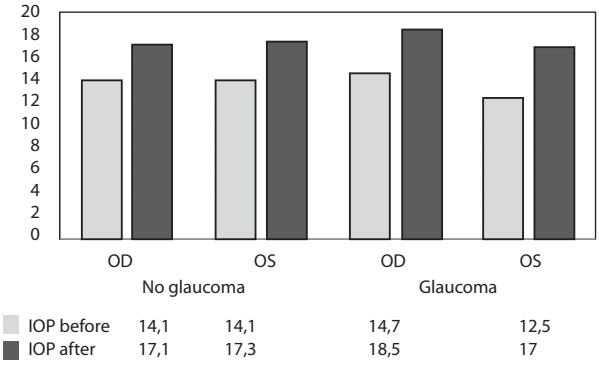

Fig. 2. Intraocular pressure changes in patients with and without glaucoma

Conflict of interest: None

REFERENCES

1. Bakri SJ, Moshfeghi DM, Rundle A, et al // IOP in eyes treated with monthly ranibizumab: A post hoc analysis of data from the MARINA and ANCHOR trials. Paper presented at: Annual meeting of the American Academy of Ophthalmology; Chicago, IL; October 15, 2010
2. Beato J.• Pedrosa A.C *et al* // Long-Term Effect of Anti-VEGF Agents on Intraocular Pressure in Age-Related Macular Degeneration. *Ophthalmic Res* 2016;56: 30-34
3. Dedania VS, Bakri SJ // Sustained elevation of intraocular pressure after intravitreal anti-VEGF agents. *Retina* 2015; 35: 841-858
4. Good TJ Kimura AE, Mandava N, Kahook MY // Sustained elevation of intraocular pressure after intravitreal injections of anti-VEGF agents. *Br J Ophthalmol* 2011; 95: 1111-1114
5. Kahook MY, Liu L, Ruzyck i P, et al // High-molecular-weight aggregates in repackaged bevacizumab. *Retina*. 2010;30:887-892
6. K Ghasemi Falavarjani and QD Nguyen // Adverse events and complications associated with intravitreal injection of anti-VEGF agents: a review of literature. *Eye* 2013; 27: 787-794
7. Liu L, Ammar DA et al // Silicone oil microdroplets and protein aggregates in repacked bevacizumab and ranibizumab: effects of long-term storage and product mishandling. *Invest Ophthalmol Vis Sci*. 2011;52:1023-1034
8. McCannel CA. Meta-analysis of endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents // *Retina* 2011; 31: 654-661
9. Nurit Mathalone, Orna Geyer // Intraocular pressure elevations following intraocular injections of anti-VEGF agents. *Retinal Physician*. 2012;9: 26-32
10. Rosenfeld PJ, Brown DM, Heier JS, et al // MARINA Study Group. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med*. 2006;355: 1419-1431
11. Scott IU, Flynn Jr, HW. Reducing the risk of endophthalmitis following intravitreal injections // *Retina* 2007; 27: 10-12

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