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INTRAVITREAL USE OF AVASTIN FOR TREATING MACULAR EDEMAS CAUSED BY THROMBOSIS OF THE CENTRAL RETINAL VEIN

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ABSTRACT

The aim of this investigation was to assess the efficacy of avastin intravitreal injection in patients with thrombosis of retinal veins.

Material and Methods: *The investigation involved 30 patients of both genders, who had retinal veins thrombosis with macular edema. The average age of patients was 57 years old. The visual acuity of patients by counting fingers near the face was up to 0.9; thickness of the macula area was from 381 μm to 958 μm. All the patients were intravitreally injected 1.25 mg avastin. The observation period was 6 months.*

Results: *In a month after avastin injection the visual acuity increased in 27 patients, while in 3 patients it remained unchanged. According to optic coherent tomography data, the average thickness of the macular area decreased by 200-400 μm in all tested patients. In 3 months after the injection visual acuity increased in 6 patients; in 21 patients it remained the same, as after the 1st injection; in 2 patients the sharpness of vision decreased, but was higher than before the injection, while in 1 patient it decreased and was worse than initially. The average thickness of the macular area, according to optic coherent tomography data, remained the same, as after the 1st injection or slightly decreased: by 10-35 μm. In 6 months after the injection, in 3 patients the visual acuity increased, as compared to outcomes observed upon the 1st injection: in 19 patients sharpness of vision remained the same; in 5 patients the visual acuity decreased, but was better than the initial one, and in 3 patients the sharpness of vision decreased to the level below the initial. On average, the thickness of macular area, according to optic coherent tomography data, remained the same, as after the 1st injection in 13.4% patients; in 73.3% patients it decreased by 19-225 μm. and in 13.3% patients the specified index increased, but the macular area was thinner than before the injection. No side-effects of avastin injections were recorded.*

Conclusion: *Intravitreal injection of avastin in patients with post-thrombotic maculopathy decreased the edema in the macular area and improved the visual function of the eye.*

Keywords: *optic coherent tomography, avastin, macula lutea, thrombosis.*

INTRODUCTION

Thromboses of retinal veins – as a rather frequent condition of the eyes – compose about 60% among all the acute vascular pathologies of the visual organ and are on the second place after diabetic retinopathy by its retinal affection severity and prognosis. In 15% cases thromboses of retinal veins underlie vision-related disability. Retinal veins occlusions cause not only a decrease of vision acuity, but also bring to such complications as neovascular glaucoma, relapsing hemorrhages, etc., as a result of which patients become disabled. lose their professional suitability at an able-bodied age [*Kiseleva T., 2001*].

In the great majority of cases with thrombosis of the central retinal vein (CRV) its branches are affected (63%-85%). The resistant cystoid macular edema, which is very difficult to treat, is a frequent

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cause of visual acuity lowering [*Parodi N. et al., 2006; Klein R. et al., 2008*].

Thromboses of retinal veins present a polyetiological disease. The increased arterial pressure, *diabetes mellitus*, atherosclerosis of vessels, diseases bringing to increased blood coagulability, *etc*. might cause this impairment.

A common way of treating thromboses of the CRV and its branches with macular edema is lasercoagulation of the macular zone by "*cancellus*" type or intravitreal introduction of corticosteroids and inhibitors of vascular endothelial growth factor (VEGF). Unfortunately, photolasercoagulation gives a positive result only in 15-20% patients with chronic macular edema. Alongside with the positive effect (temporary improvement of vision) corticosteroids increase intraocular pressure up to 35-40 *mm Hg* in 30-40% patients and thus bring to cataract progressing [*Vardanyan A., Abgaryan L., 2008*].

Avastin (bevacizumab) is a recombinant, hyperchimeric (humanized, approximated to human) monoclonal antibody, which is selectively binding with biologically active VEGF and neutralizes it. Avastin inhibits VEGF binding with its receptors on the endothelial cells surface, which brings to a decrease of vascularization. Avastin is composed of 214 amino acids and has molecular weight of about 149,000 daltons.

Since 2004, this preparation has been actively used in oncology for treating cancers of the large intestine and rectum, and already since 2005 specialists has begun to use avastin in ophthalmology. American researchers reported about the first experience of using avastin in patients with exudative type age-related macular degeneration [*Rosenfeld P. et al., 2006*].

Taking into account the above mentioned, the aim of our work was to reveal the efficacy of intravitreal use of avastin in patients with retinal veins occlusion.

Material and Methods

From 2010 to 2011, 30 patients (both genders) with occlusion of retinal veins and macular edema made the Study Group managed at the Traumatological Department of the Ophthalmological Center after S.V. Malayan. The average age of patients was 57 years old. The visual acuity of patients by counting fingers near the face was up to 0.9; thickness of the macula area was from 381 *μm* to 958 μm. All the patients were intravitreously injected 1.25 *mg* avastin ("Roche", Sweden). The patients were observed for 6 months.

During each visit the visual acuity of patients was checked by Sivtsev's table, Maklakov tonometry [*Bakbardin Yu., Kondratenko Yu., 1997*], biomicroscopy by slit lamp "CE Video Omega 2c" ("Heine", Germany), indirect ophthalmoscopy *via* "SC-5D" ophthalmoscope with a wide pupil ("Topcon Corporation", Japan) were also done. The optic coherence tomography (OCT) with the help of "Stratus OCT 4.0.2" ("Zeiss", Germany) and eye fundus photography (AX50) using fundus camera "Topcon" ("Topcon Corporation", Japan) were carried out before treatment and 1, 3, 6 months later.

According to the visual acuity 4 groups of patients were formed:

- I group: visual acuity by counting fingers near the face made up to 0.01 (4 patients);
- II group: visual acuity – from 0.07 to 0.09 (4 patients);
- III group: visual acuity – from 0.1 to 0.4 (19 patients);
- IV group: visual acuity – from 0.6 to 0.9 (3 patients).

The average thickness of the retina macular area was measured using OCT and, appropriately, made:

- 958 μm in the I group;
- 815 μm in the II group;
- 533 μm in the III group;
- 381 μm in the IV group.

Intravitreal injection technique: After local anesthesia with 1% tetracaine solution ("Liqvorpharmaceuticals", Armenia) the conjunctival cavity was washed with 10% betadin solution ("ArpiMed", Armenia). Then with the help of disposable 0.5 *ml* syringe with a 30 *gauge* needle receding from the *limbus* by 3-4 *mm* 0.05 *ml* of solution containing 1.25 *mg* avastin was slowly (during 3-4 seconds) introduced intravitreously. Upon the injection. 10% betadin solution. 0.5% "Oftaquix" eye drops ("Santen", Finland) were dropped into the conjunctival cavity and a light massage of the eyeball was done during 1-2 minutes to normalize the intraocular pressure. Then the eye fundus was examined until the restoration of retinal vessels related circulation. As a preventive means against the inflammatory process the patients were administered anti-inflammatory eye drops: "Oftaquix", "Oftan dexamethasone" ("Santen", Finland) for 7 days. The patients were examined the day after injection.

The patients, who received avastin intravitreal

injection, stated minimal discomfort after the procedure; sometimes they had dimmed vision, burning sensation in the eye. No ophthalmohypertension was noted in any of the patients. Circulation in the retinal vessels was restored within 5 minutes. No patient needed paracentesis.

Results

The findings on tested visual acuity in patients were summarized and presented as Table 1.

Table 1.

Changes in average visual acuity according to groups of patients

Patients	before avastin injection	Period of investigation after treatment (in months)		
		1	3	6
I group	0.015	0.03	0.025	0.015
II group	0.08	0.5	0.5	0.42
III group	0.25	0.6	0.5	0.5
IV group	0.7	1.0	0.7	0.7

In a month after avastin injection the visual acuity increased in 27 patients; in 3 patients it remained unchanged.

In 3 months after the injection visual acuity in 21 patients remained the same, as after the 1st injection; in 6 patients the sharpness of vision increased, while in 2 patients it decreased, as compared to the 1st injection outcomes, but was better than before avastin administration; only in 1 patient the visual acuity turned to the worse.

In 6 months after the injection, the visual acuity in 19 patients remained the same, as compared to the results of the 1st injection; in 3 patients the sharpness of vision increased, in 5 patients it decreased becoming worse than after the 1st injection, but was better than the initial one; in 3 patients the visual acuity decreased, as compared to the state before the injection.

It should be emphasized that on average the visual acuity of patients made 0.7; in 1 patient it decreased up to 0.2 and became worse than the initial one; in 2 patients it remained the same, as after the 1st injection (visual acuity: 1.0).

The results of studies on the thickness of retina were summarized and presented as Table 2.

Table 2.

Changes in average thickness of retinomacular area according to groups of patients (μm)

Patients	before avastin injection	Period of investigation after treatment (in months)		
		1	3	6
I group	958	544	547	677
II group	815	444	443	443
III group	533	429	394	244
IV group	381	179	166	166

Considering that in healthy people the thickness of retina is about 180-240 *μm* a conclusion might be drawn that at the moment of admission to the hospital the retina thicknesses in patients of all groups was above the norm. In fact, the highest indices were in the first group and the lowest ones in the fourth group. In 1 month after avastin injection the thickness of retina decreased in 27 patients, while in 3 patients it remained unchanged.

In 3 months after injection the thickness of retina remained the same, as after the 1st injection in 23 patients; in 6 patients the studied index decreased, and only in 1 patient it became worse (thicker) than prior to injection.

In 6 months the thickness of retinomacular area remained the same, as after the 1st injection in 23 patients; in 3 patients it decreased even more, while in 3 other patients it became worse. as compared to the 1st injection, though the state was better than prior to injection. Only in 1 patient the thickness of retinomacular area increased, and it became thicker than before injection.

In the first group of patients the thickness of retina anew increased within 6 months in comparison with the previous observation, which was acompained with the fall of the visual acuity; this latter means that the effect of avastin is temporal.

It is important to mention that depending on the retina thickness the patient belongs to the second or third group, with the visual acuity, which is bad enough. Consenquently, the treatment with avastin should be protracted.

In the second group of patients, the retina thickness goes down in 6-month term, but it is still higher than the normal range, in parallel with the stabilized increase of the visual acuity, which means that avastin is effective, but not permanently.

In the third group the retina thickness decreased

permanently until the norm acompained with the increase of visual acuity. Thus, it might be concluded that the influence of avastin is effective, but not always.

In the fourth group, we can mention the abrupt fall of the retina thickness until the normal values in parallel with the increasing of visual acuity during one month and subsequent worsening of the previous treatment results. Hence, we can say that in this group avastin is effective as well.

Conclusion

Taking into account the above-mentioned, a conclusion might be drawn that 1.25 *mg* avastin intravitreal injection is an effective means for treatment of post-thrombotic macular edemas, as well as a preventive means for post-thrombotic secondary glaucomas. Thus, this procedure can be implemented in the clinical practice of post-thrombotic maculopathy management.

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