

The effect of intravitreal bevacizumab on visual acuity in exudative form of age-related macular degeneration treatments

Učinek intravitrealne primjene bevacizumaba na vidnu oštrinu u eksudativnoj formi liječenja senilne makularne degeneracije, povezan s godinama starosti

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Summary

The aim of the research is to determine whether intravitreal bevacizumab improves the visual acuity significance in treatment of patients with exudative form of age-related macular degeneration.

Patients and methods: This study included 45 patients, 75 eyes with senile degeneration of the macula lutea, who were treated in Prim. dr. Abdulah Nakas General Hospital during the period from November 2007 - November 2010. The criteria for inclusion of patients in the study were that they had clinical signs of age-related degeneration of macula lutea with diagnostic methods verifying the changes in the retina, and aged between 55 and 75 years.

Result: The average age of patients treated with bevacizumab was 71.27 years (71 years, 3 months and 7 days). The study included 28 female patients and 17 male patients. There was a statistically significant difference ($p < 0.05$) in visual acuity between any measurement period. The smallest difference was between 4 and 6 months but still statistically significant. If we analyze the trend line, we can conclude that it is logarithmic, which shows that there is a trend of improvement.

Conclusion: The results of the application of bevacizumab intravitreally in age-related degeneration of the macula lutea showed that intravitreal bevacizumab for exudative form of age-related macular degeneration improved the visual function of patients, which significantly affected the extension of their active life expectancy.

Ključne riječi: bevacizumab, visual acuity, macular degeneration

Sažetak

Cilj istraživanja je ustanoviti poboljšava li intravitrealna primjena Bevacizumaba vidnu oštrinu pacijenata pri liječenju eksudativne forme senilne makularne degeneracije.

Ispitanici i metode: U ovu studiju je uključeno 45 pacijenata, 75 očiju, koji imaju senilnu degeneraciju makule lutee, a koji su tretirani u Općoj bolnici, "Prim. dr. Abdulah Nakaš", u razdoblju od studenoga 2007. do studenoga 2010. godine. Kriterij za uključivanje pacijenata u studiju su bili pacijenti koji imaju kliničke simptome senilne degeneracije makule lutee s dijagnostičkim metodama verificiranim promjenama na retini, starosne dobi između 55 i 75 godina.

Rezultat: Prosječna dob pacijenata tretiranih Bevacizumabom je 71,27 godina (71 godina, 3 mjeseca i 7 dana). U studiju je uključeno 28 pacijenata ženskoga spola, te 17 pacijenata muškoga spola. Postoji statistički značajna razlika ($p < 0,05$) za vidnu oštrinu između bilo kojeg razdoblja mjerenja. Razlika je najmanja između 4 i 6 mjeseci, ali je i dalje statistički značajna. Ako analiziramo liniju trenda možemo zaključiti da je ona logaritamska, odnosno pokazuje da postoji trend poboljšanja.

Zaključak: Na osnovu dobijenih rezultata u primjeni Bevacizumaba intravitrealno kod senilne degeneracije makule lutee, utvrđeno je da intravitrealna primjena Bevacizumaba kod eksudativne forme senilne makularne degeneracije poboljšava vidne funkcije pacijenata, što značajno utječe na produljenje njihove aktivne životne dobi.

Key words: bevacizumab, vidna oštrina, senilna degeneracija makule lutee

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Introduction

Senile macular degeneration, in the world today, is a leading cause of vision impairment and blindness of the elderly population. Dry senile degeneration is a lighter form of macular degeneration, and the preliminary stage of development of severe exudative form. We are trying to maintain visual function by combining antioxidant therapy, argon laser photocoagulation PDT, Kenalog and inhibitors of vascular endothelial growth factor.

After the injection of bevacizumab, some patients can expect improved vision, and some the slowing down or stopping of further vision deterioration in the eye of the affected, which depends on the duration of the illness.

Growth Factor Blockers Therapy (anti-VEGF)

The most modern and most recent AMD treatment modality involves the application of drugs directly injected in the vitreous area of the eye.^{1,2}

The following are used:

- Avastin (Bevacizumab) 1.25 mg (0.05 ml) in three doses every two months.
- Lucentis (Ranibizumab) 0.5 mg 1x a month for three months.
- Macugen (Pegaptanib sodium) 0.3 mg in three doses every six weeks.

Objective research

The aim of the research is to determine whether intravitreal bevacizumab improves the visual acuity significance in the treatment of patients with exudative form of age-related macular degeneration.

Material and methods

The study was conducted as a retrospective prospective clinical, manipulative control study. This study included 45 patients, 75 eyes with senile degeneration of the macula lutea, who were treated in "Prim. dr. Abdulah Nakas" General Hospital during the period from November 2007 – November 2010. The criteria for the inclusion of patients in the study were that the patients had clinical signs of age-related degeneration of macula lutea with diagnostic methods verifying the changes in the retina, and aged between 55 and 75. The criteria for exclusion of the patients from the study: patients who had some other form of the eye disease.

Bevacizumab intravitreally

The intravitreal injection of Bevacizumab represents direct application of the medicine in the eye in a spot where the highest concentration and the strongest effect of the medicine is ensured.^{3,4,5} 1.25 mg bevacizumab intravitreally (0.05 ml) is applied.

The procedure is virtually painless, because a very thin and small 27 G needle is used, and the eye is previously anaesthetized by anesthetic drops, salt tetracaine 2x. The procedure is performed in the operating room due to complete sterility. It is measured by caliper, and it is given 3.5 mm from the limbus through the pars plana.

In the first few days after the surgery, the patient can see floaters floating before the eye. Over time, usually in 1-3 months, the cure dissolves completely. The following complications may occur in a small percentage:

- suffusions in the bulbar conjunctiva^{6,7}
- bleeding (haemophthalmus)^{8,9}
- increased intraocular pressure^{10,11}
- peeling of the internal membrane of the eye^{12,13}
- infection (endophthalmitis)^{14,15,16}
- rupture of the retina and horioida¹⁷.

Follow-up examinations

After the application of the drug, patients use antibiotic drops Tobrex salt 4x for five days. The patients are told that they will see floaters floating before the eye in the first few days after surgery. It is a remedy in the vitreous of the eye that quickly settles to the bottom of the eyeball, and it does not cause any further difficulty.

Visual acuity

The visual acuity for distance is examined in all patients with a correction before giving bevacizumab, 2 months after the application of the first dose, 4 months after the application of the second dose, and 6 months after the application of the third dose.

Results

Bevacizumab treatment was provided to 45 patients, 75 eyes. Of these, 36 patients were treated for the right eye and 39 were treated for the left eye. In 30 patients, both eyes were treated with bevacizumab, in 6 patients just the right eye, and in 9 patients only the left eye were treated (Table 1).

Table 1 Avastin application

Tablica 1. Primjena Avastina

Right eye <i>Desno oko</i>	Left eye <i>Lijevo oko</i>	Total <i>Sveukupno</i>
36	39	75

Table 2 Gender and age structure

Tablica 2. Spol i starost

Structure <i>Struktura</i>	Female <i>Žensko</i>	Male <i>Muško</i>	Total <i>Sveukupno</i>
Gender <i>Spol</i>	28	17	45
Age <i>Starost</i>	71.18	71.41	71.27

The average age of the patients was 71.27 years (Table 2). There was a statistically significant difference ($p < 0.05$) in visual acuity between any measurement period. The smallest difference was between 4 and 6 months, but it was still statistically significant. If we analyze the trend line, we can conclude that the trend line is logarithmic, and that it shows a decreasing trend of improvement between the second and third doses of bevacizumab (Table 3).

Table 3 Average visual acuity

Tablica 3. Prosječna oštrina vida

Start of therapy <i>Početak terapije</i>	First dose <i>1. doza</i>	Second dose <i>2. doza</i>	Third dose <i>3. doza</i>
0.16	0.21	0.25	0.26

Table 4 Visual acuity

Tablica 4. Oštrina vida

Period of use <i>Vrijeme uporabe</i>	VOD	VOS
Before Avastin therapy <i>Prije terapije Avastinom</i>	0.15	0.17
After the first dose <i>Nakon prve doze</i>	0.21	0.21
After the second dose <i>Nakon druge doze</i>	0.26	0.24
After the third dose <i>Nakon treće doze</i>	0.27	0.25

Discussion

This study included 45 patients who were treated in the Ophthalmology Department of Prim dr Abdulah Nakas General Hospital. Bevacizumab treatment was provided to 45 patients, 75 eyes. Of these, 36 patients were treated on the right eye and 39 on the left eye. In 30 patients both eyes were treated with bevacizumab, in 6 patients just the right eye, and in 9 just the left eye.

The average age of patients treated with bevacizumab was 71.27 years (71 years, 3 months and 7 days). Avastin treatment is safe and effective for exudative AMD. It is not necessary to give an injection every month, the effect of the injection lasts for at least eight weeks. The average age of patients was 74.3 years. Visual acuity improved from 0.08 to 0.2, and there is a reduction in central retinal thickness.¹⁹

Lazic, Gabric reported patients with average age 74.8 (61-85) years, increase in visual acuity of 1.29 lines, $p = 0.001$.²⁰ Ruppenstein at al study included 73 eyes that were treated with 1.25 mg of Avastin intravitreally. After 30 weeks, visual acuity increased by one line.²¹ Intravitreal application of Avastin led to a significant improvement in visual acuity of 2.2 lines.²²

There was a statistically significant difference ($p < 0.05$) in visual acuity between any measurement period. The smallest difference was between 4 and 6 months, but still statistically significant. Carneiro and colleagues, best corrected visual acuity was improved and central retinal thickness decreased.²³ Weigert and colleagues, visual acuity improved by 2.2 lines at 6 months follow-up.²⁴ Subramanian and associates, visual acuity improved by 2 lines after a year of monitoring.²⁵

Singh and colleagues examined visual acuity in 73 eyes during a period of 6 months. After three months, visual acuity improved by 1 line, and after 6 months by 2 lines.²⁶ Wolfgang and associates, in 18 patients (56%) visual acuity improved by 3 lines, in 9 patients (28%) visual acuity did not change and in 5 cases (16%) there was a decrease in visual acuity by 1 line.

Conclusion

The study included a total of 45 patients, 75 eyes. Of these, 17 patients were male and 28 female patients. 30 patients received bevacizumab in both eyes, and 15 patients in one eye. 36 right and 39 left eyes were treated. The age of the patients was 71.27 years.

Visual acuity was with statistically significant difference in any measurement period. Visual acuity improved by 1 line, from 0.15 to 0.25. Based on the results obtained in the application of bevacizumab

intra-vitreally in age-related degeneration of macula lutea, the following conclusion is derived: The first application of intravitreal bevacizumab for exudative form of age-related macular degeneration improved visual function of patients, which significantly affected the extension of their active life expectancy.

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