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Original Research Paper

Medicine

THE EFFICACY OF TREATMENT WITH AFLIBERCEPT INTRAVITREAL INJECTIONS IN PATIENTS WITH WET AGE-RELATED MACULAR DEGENERATION".

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ABSTRACT

Purpose: The aim of this study was to evaluate the effectiveness and safety of treatment with aflibercept administered intravitreally in patients with neovascular age-related macular degeneration after first year of treatment. Moreover, the influence of following factors on therapeutic success with aflibercept was investigated: CNV type, lens status (pseudophakic vs phakic), patient's age, sex and the fact if patient was previously receiving anty-VEGF injections. **Methods:** A prospective clinical study was conducted on 90 eyes of patients (age 56 to 89 years old, 50 females, 40 males) who were diagnosed with choroidal neovascularisation (CNV) due to wet AMD. Before each injection best corrected visual acuity(BCVA) on Snellen chart, converted then to ETDRS scale for statistical purposes and central retinal thickness (CRT) using optical coherence tomography (OCT) were assessed. All patients received 3 doses of 2,0 mg intravitreal aflibercept every 4 weeks, followed by aflibercept injections every 2 months. The primary endpoint of the study was determined on best corrected visual acuity (BCVA) and changes observed in central retinal thickness (CRT) 3 months and 1 year after treatment with aflibercept comparing with BCVA and OCT at the baseline. **Results:** After the first year of treatment with aflibercept a statistically significant improvement of mean BCVA was observed. The patients gained +2,47 letters (Z=-1,989; p<0,05) after 3 months and +9,29 letters (Z=-6,812; p<0,001) in ETDRS scale after 52 weeks of treatment. At the same time a statistically significant reduction of CRT in OCT was observed. The mean CRT decreased from 370,38 µm to 300,76µm after 52 weeks of treatment (p<0,001). Intravitreal injections were well tolerated and no serious local or general adverse events were recorded. The baseline visual acuity was the most important predictor for final BCVA after the treatment (r=-0,421; p<0,01). The subtype of CNV, patient`s sex, lens status (phakic vs pseudophakic) and therapy type (previous anty-VEGF treatment vs treatment-naïve patients) did not correlate with final BCVA. **Conclusions:** The intravitreal therapy with aflibercept is effective and safe for treating patients with wet AMD in routine daily practice. The obtained results proves the efficacy of treatment with aflibercept in patients with wet AMD and indicate the importance of early diagnose and treatment implementation to obtain the best functional and morphological results.

KEYWORDS : VEGF, aflibercept, wet age-related macular degeneration

Introduction:

Age-related macular degeneration (AMD) is one of the main causes of the irreversible loss of central vision in the population over 50 years of age in developed countries. [1-5] This disease is a huge social problem which came to be called an epidemic of blindness in the XXI century. According to statistical data, age-related macular degeneration currently affects 8.7% of the world's population. [6] It is a chronic disease with complex and multifactorial pathogenesis, and the incidence increases with age. [7-8] It is believed that both genetic and environmental factors influence the development of this disease. [9] The known risk factors include: age, female sex, white race, family history of AMD, bright blue colour of iris, cardiovascular diseases, arterial hypertension, cigarette smoking, intensive exposure to visible light and UV radiation and dietary antioxidant deficiency. [10] There are two forms of AMD: dry and exudative (wet). The dry form constitutes 90% of cases and is characterized by a slow course with a gradual decrease in visual acuity. In advanced cases, as a result of atrophy of the central retina and so called geographical atrophy, the dry form may lead to a significant loss of central vision. So far, there is no therapy of AMD dry form and geographical atrophy. The only available treatment exist for exudative form. The exudative form occurs in 10-15% of AMD patients and is characterized by a more dangerous and dynamic course, which in a short time may lead to irreversible loss of central visual acuity as a result of haemorrhage to the central retina with subsequent scarring. [11] The exudative form of AMD is responsible for 80% of cases of significant vision loss. [12] Patients with AMD complain mainly about deterioration of visual acuity, decreased contrast, deterioration of colour vision, problems with reading or performing activities requiring precise vision, as well as difficulties with facial recognition and wavy lines i.e. metamorphopsy and distorted vision with scotoma in the center.

In Poland, according to the AMD Association, about 1.5 million people suffer from age-related macular degeneration, of which about 200,000 people have diagnosed with wet AMD, and each year this group increases by another 10-15,000 patients. [13-14] In the next 25 years, the number of cases is to triple, which is related to the ageing of the population. [11]

Age-related macular degeneration develops within the outer retina layers (photoreceptors, pigment epithelium, Bruch membrane) and adjacent vascular capillaries, with retinal pigment epithelium-RPE in the central place in AMD pathogenesis. The disease is associated with the presence of choroidal neovascularization (CNV). The neovascular membrane is caused by excessive expression of vascular endothelial growth factor (VEGF) and imbalance between stimulating factors and angiogenesis inhibitors. [15-19] The oxidative stress factors, local inflammatory reaction in the retina, complement activation with consequent release of the VEGF-A factor, which shows affinity to the two tyrosine kinase receptors present on endothelial cells (VEGFR-1 and VEGFR-2), are leading to activation of angiogenesis. [20-26] At a later stage comes to the proliferation of new vessels from the choriocapillaries of the choroid, which results in the formation of neovascular membrane. Leakage of plasma components from the neovascular membrane, lack of nutrients and gradual scar formation causes the death of photoreceptors. [27-28]

One of the revolutionary achievements of ophthalmology of the last decade was the introduction of endothelial growth factor inhibitors (anti-VEGF) administered intravitreally for the treatment of wet AMD. In 2006, ranibizumab (Lucentis, Genetech USA, Inc.), which is a fragment of the humanized monoclonal antibody binding all VEGF-A isoforms with affinity 100 times greater than bevacizumab, was approved for treatment of wet AMD. Moreover, it is characterized by shorter half-life in the bloodstream, better penetration into the retina and lower inflammatory response potential compared to bevacizumab. [29]

In 2011, aflibercept (Eylea, Regeneron Pharmaceutical Inc. & Bayer, Basel, Switzerland), which is a recombinant fusion protein (110 kDa) composed of extracellular domain fragments of VEGFR1 and VEGFR2 receptors combined with a fragment Fc of human immunoglobulin IgG1 group was approved for treatment of wet AMD. [30] The effect of aflibercept consists in binding all isoforms VEGF-A, VEGF-B and Placental Growth Factor-PIGF, which, as it has been proved, also contributes to the formation of CNV membrane. [31] Aflibercept is characterized by higher binding affinity of VEGF factor than bevacizumab and ranibizumab. [32-34] This allows effective blocking of VEGF factor with lower drug concentration and a longer half-life, which involves the possibility of extending the intervals between injections. [34] The treatment regimen as recommended is to administer aflibercept 2.0 mg in the form of intravitreal injections every 4 weeks in the first three months of therapy and then continue to administer the injections at intervals of 8 weeks in the first year of treatment. [35] The results of clinical trials confirmed the high efficacy and safety of both registered medications, ranibizumab and aflibercept, in the treatment of wet age-related macular degeneration. Phase III studies of ANCHOR, MARINA, VIEW1 and VIEW2 showed that in 90-96% of patients receiving systematic intravitreal injections of ranibizumab and aflibercept, it was possible to stop the disease progress and improve visual acuity during the two-year observation period. [35-37] Treatment with intravitreal injections of ranibizumab and aflibercept is the gold standard of therapy in wet age-related macular degeneration.

Purpose

The randomized control studies on wet AMD confirm the effectiveness of treatment with aflibercept. However, the results of clinical trials are not always reflected in everyday clinical practice. In addition, the literature continues to study intensively the factors allowing to predict the response to therapy in patients with nAMD.The aim of the study is to evaluate the effectiveness and safety of aflibercept treatment after the first year of therapy. The main endpoint is to evaluate the improvement of best corrected visual acuity (BCVA) and changes in central retinal thickness (CRT) in optical coherence tomography (OCT) after 3 months and after a year of treatment with aflibercept in relation to baseline BCVA and CRT.Moreover, the paper is an attempt to answer the question what factors may modify the answer to anti-VEGF therapy. The influence of the following factors on the effectiveness of aflibercept therapy was analyzed: type of neovascular membrane, lens status (phakic vs pseudophakic), age, gender and the fact whether the patient had received anti-VEGF injections before the start of the study. The occurrence of local and general adverse effects during aflibercept therapy was also observed.

Materials and methods

The study included 90 eyes of patients aged 56 to 89 years, in whom active choroidal neovascular membrane (CNV) in course of wet age-related macular degeneration was diagnosed by means of fluorescein angiography (FA) and optical coherence tomography (OCT). The patients were treated with anti-VEGF intravitreal injections at the Prof. K. Gibi ski University Clinical Centre in Katowice, Poland. Table 1 shows the patient characteristics.

Table 1. Patient characteristics.

Characteristic	Value
Number of patients	90 (50 female, 40 male)
Age in years (Mean [range])	74.4 [56 – 89]
Baseline BCVA in ETDRS (Mean ± SD)	59.88 ± 14.1
Baseline CRT in µm (Mean ± SD)	370,38 ± 81,4
Number of CNV type (classic, occult, mixed)	4 vs 61vs 25
Number of pseudophakic vs phakic eyes	17 vs 73

The criteria for inclusion in the study group were as follows: presence of active, classical, occult or mixed neovascularization membrane (CNV) occupying more than 50% of the AMD lesion confirmed by OCT and fluorescein angiography examination, age 45+, lesion size less than 12 DA (12 areas of the optic disc), the best corrected visual acuity (BCVA) in the treated eye between 0.1-0.8 determined according to the Snellen charts, patient's written consent for participation in the study, an improvement in visual acuity in relation to the initial BCVA, stabilisation of BCVA or a deterioration of BCVA (≤3 rows according to the Snellen charts at any control point). The exclusion criteria were as follows: hypersensitivity to aflibercept or to any of the excipients, presence of intraocular inflammation, pregnancy or breastfeeding, rhegmatogenous retinal detachment, stage 3 or 4 macular hole, lack of patient's compliance, progression of a disease defined as a deterioration of BCVA to < 0,1 as defined in the Snellen charts for more than two months, presence of permanent damage to the structure of the fovea (significant damage to the structure is defined as current fibrosis or atrophy in or a significant chronic scar), dominant geographic atrophy, predominant subretinal haemorrhage, loss of BCVA at any control point by more than 3 rows according to the Snellen charts.

The study obtained a positive opinion of the Bioethics Committee by Resolution No. KNW/0022/KB1/38//III/15/16 of 29.11.2016 of the Bioethics Committee of the Medical University of Silesia in Katowice. All patients provided written informed consent and this study was conducted in accordance with The Declaration of Helsinki. Before each injection each patient underwent a comprehensive ophthalmic exam, including measurement of best corrected visual acuity (BCVA) using Snellen charts, which was then converted into the ETDRS equivalent, slit-lamp biomicroscopy with dilated funduscopy, Goldman applanation tonometry and cross-sectional OCT images using a commercial SD-OCT system (TOPCON 3D OCT 2000) for imaging.The main endpoint was the evaluation of changes in central retina thickness (CRT) and best corrected visual acuity (BCVA) after the first 3 months and after a year of anti-VEGF injection treatment in relation to initial BCVA and CRT. The recommended dose of aflibercept is 2 mg, which corresponds to 50 microlitres of solution (0.05ml) per one intravitreal injection. Aflibercept treatment was started with one injection per month for three consecutive months, followed by one injection every 2 months. In total, each patient received 7 doses of aflibercept during the first year of treatment. The observation period was 12 months.

Statistical analysis of the results was carried out using the IBM SPSS Statistics software. Due to the size of the study group (n=90), compliance with the normal distribution of individual variables was performed using the Shapiro-Wilk test. Since the examined variables did not have normal distribution, the following non-parametric tests were used in further analysis: Wilcoxon's test for dependent samples (marked ranks test), Mann Whitney's U test for testing differences between two groups and Kruskal-Wallis' test for testing differences between more than two groups. Pearson's correlation coefficient (r) was used to investigate correlations between the compared

variables. The results were assumed to be statistically significant at value of $p \leq 0.05$.

Results

Best corrected visual acuity

The results of the statistical analysis showed that the best corrected visual acuity after administration of 3 injections of aflibercept increased (x =62.35; SD=13.89) comparing to the first measurement (x =59.88; SD=14.08) before administration of the drug. Analysis of Wilcoxon's marked ranks test showed that this difference is statistically significant, Z=-1.989; p<0.05. An average improvement in the best corrected visual acuity after 3 injections of +2.47 letters on the ETDRS scale was observed.

The statistical analysis showed a significant improvement in the best corrected visual acuity after a year of treatment with aflibercept. The best corrected visual acuity of ETDRS after 7 injections was higher (x =69.17; SD=9.57) than in the first measurement (x =59.88; SD=14.08) before administration of the drug. Analysis of Wilcoxon's marked ranks showed that the difference was statistically significant Z=-6.812; p<0.001. The average improvement in best corrected visual acuity by 9.29 letters on the ETDRS scale after 7 aflibercept injections after the first year of treatment was demonstrated.

The graph below shows changes in mean visual acuity according to the ETDRS scale before administration of the drug, after 3 injections and after 7 aflibercept injections, respectively. (Fig.1.)

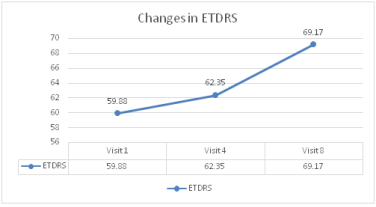


Fig.1. Best corrected visual acuity on the ETDRS scale in patients with wet AMD treated with aflibercept, before therapy (Visit 1), after 3 injections of aflibercept (Visit 4) and after 7 injections of aflibercept (Visit 8).

Central retinal thickness (CRT)

The thickness of the central retina (in μm) was evaluated by optical coherence tomography OCT before 1 injection of aflibercept (CRT_0), then after 3 injections (CRT_4) and after 7 injections (CRT_8). The results of the statistical analysis showed that the central retinal thickness CRT after 3 injections was lower (x =301.57; SD=49.28) than in the first measurement (x =370.38; SD=81.39). The analysis of Wilcoxon's ranged signs appear to prove that this difference is statistically significant, Z=-6.903; p<0.001. The mean decrease in central retinal thickness of CRT by 68.81 μm after 3 aflibercept injections at monthly intervals was demonstrated. In 11 patients (12.22%) the CRT increased. Decrease of central retinal thickness CRT was observed in 79 patients (87.78%).CRT after 7 injections was lower (x =300.76; SD=41.7) than in the first measurement (x =370.38; SD=81.39). The analysis of Wilcoxon's ranged signs showed that the difference was statistically significant, Z=-6.862; p<0.001. After 7 injections of aflibercept, an average decrease of 69.62 μm in the central retinal thickness of CRT was observed compared to the measurement of CRT before treatment. Eventually, an increase in CRT was observed in 14 patients (15.56%), no changes in 1 person (1.11%) and an improvement in CRT (decrease) in 75 patients (83.33%).

The graph below shows the changes in the thickness of CRT after successive injections. The highest decrease in CRT was achieved after the first 3 injections (Visit 4), and after the next 4 doses of aflibercept (Visit 8) a slight further decrease in retinal thickness was achieved, which stabilizes the obtained morphological effect. (Fig.2.).

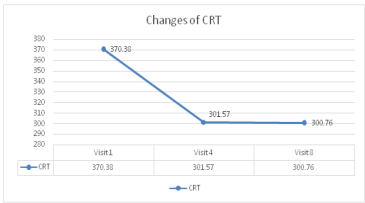


Fig.2. Changes in the central thickness of the retina CRT after successive injections (Visit 1 - before administration of the first dose, Visit 4 - after 3 injections of aflibercept, Visit 8 - after 7 injections of aflibercept).

Correlation between the best corrected visual acuity BCVA before therapy initiation and the best corrected visual acuity BCVA after 7 injections of the aflibercept.

After the Pearson correlation analysis, it was found that there is a statistically significant negative relationship between BCVA before therapy initiation and the improvement of the best corrected visual acuity one year after aflibercept treatment, i.e. after 7 injections (r=-0.421; p<0.01), the correlation is of moderate strength . In order to investigate what improvement in the best corrected visual acuity was achieved in patients after aflibercept treatment depending on the initial best corrected visual acuity according to the ETDRS scale, patients were divided into 3 groups. Patients with the lowest initial visual acuity, i.e. between 0.1 and 0.2 according to the Snellen charts (35-50 letters on the ETDRS scale). The second group includes patients with moderate initial visual acuity: from 0.3 to 0.5 according to Snellen tables (59-70 ETDRS letters). The third group consists of patients with the highest initial visual acuity, i.e. BCVA between 0.6 and 0.8 according to Snellen charts (74-80 ETDRS letters).

The following graph shows the changes in the best corrected visual acuity in ETDRS scale with respect to the baseline ETDRS level in all three groups (Fig.3).

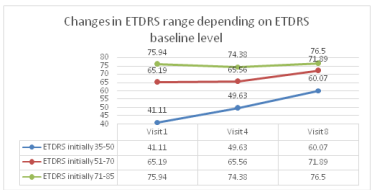


Fig.3. Changes in the best corrected visual acuity in ETDRS scale depending on the initial ETDRS (Visit 1 - before therapy, Visit 4 - after 3 injections of an aflibercept, Visit 8 - after 7 injections of an aflibercept).

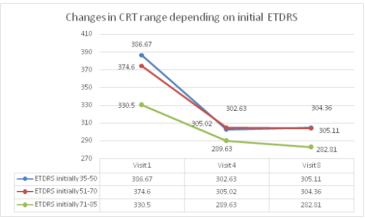
On the basis of the statistical analysis and the presented graphic, it was shown, that the greatest improvement in the best corrected visual acuity was achieved by patients in the group with the lowest initial number of ETDRS letters (35-40). The average initial ETDRS in this group was 41.11 letters , while after 7 injections the best corrected visual acuity was significantly improved and increased to the average number of letters 60.07 on the ETDRS scale. The group with intermediate best corrected visual acuity (51-70 letters on the ETDRS scale) achieved a moderate improvement in best corrected visual acuity. The average initial number of letters in this group was 65.29 on the ETDRS scale and improved to 71.89 letters. In the group of patients with the highest initial visual acuity before treatment (ETDRS 71-85), the average initial letter count was 75.94 on the ETDRS scale and improved to an average of 76.5 letters after a year of therapy.

Results of the Pearson correlation analysis showed a

significant but very low positive correlation between CRT reduction and BCVA improvement (r=0.25; p<0.05) after one year of treatment with aflibercept injections. This means that the greater the difference in the CRT range, the greater in BCVA, but at a very low level.

Figure 4 shows changes in the central retinal thickness depending on the initial level of the best corrected visual acuity in ETDRS scale. Patients were divided into 3 groups depending on the initial number of letters in ETDRS (Fig.4.).

Fig.4. Changes in the average central retinal thickness CRT depending on the initial visual acuity in ETDRS scale.



It was observed that patients with the highest initial visual acuity on the ETDRS scale (71-85 letters) had the lowest mean central retinal CRT thickness before treatment (330.5 μm). Patients in this group achieved CRT reduction after 7 injections to the mean value of 282.81 μm, i.e. by 47.69 μm on average. Patients in the group with the lowest initial visual acuity on the ETDRS scale (35-50 letters) were characterized by a higher mean central retina CRT thickness of 386.67 μm than in the other 2 groups (Visit 1). Patients from this group achieved the highest reduction of central retina thickness after 7 injections to 305.11 μm (decrease in CRT by 81.56 μm on average).

Influence of the therapy type (new vs. previous anty-VEGF) on the BCVA change after aflibercept treatment.

Among of 90 eyes, 22 were patients who had previously received anti-VEGF intravitreal injections (group marked "continuation") before starting treatment. The majority (68 individuals) were patients who had never received an anti-VEGF injection before (the group referred to as "new").The analysis showed no statistically significant differences between the results in the improvement of best corrected visual acuity between the group of patients who continued the therapy, i.e. had previously received anti-VEGF injections, and the treatment-naïve group (Z=-1,667, p<0,096).

Influence of the patient's lens (phakic vs. pseudophakic) on the change in BCVA in patients after 1 year of treatment with aflibercept.

In the analyzed group of 90 eyes, 17 eyes were pseudophakic and 73 were phakic. In the group of phakic patients at the beginning of the treatment the degree of opacity of the lens was initial or medium, i.e. good fundus view, not hindering the implementation of the OCT examination and not requiring undertaking cataract surgery in the first year of aflibercept treatment. The analysis (U Mann-Whitney, Wilcoxon) showed that there were no statistically significant differences in the BCVA between pseudophakic and phakic eyes (Z=-0,343, p<0,732).

Influence of neovascular membrane type (classical, occult, mixed) on the change of the BCVA.

The type of neovascular membrane (CNV) in the course of nAMD was determined before beginning of treatment by fluorescein angiography (AF) and OCT. 61 eyes were diagnosed as occult CNV, 25 as mixed, and in 4 cases the classic neovascular membrane was diagnosed. The conducted analysis (chi-square) showed no statistically significant differences in BCVA between the groups with mixed, classic and occult neovascular membrane types (χ 2 =2,003; p<0,367).

Influence of patient age on the change in BCVA.

The analysis showed that the patient's age correlates significantly with the changes in BCVA, but these are very weak negative correlations and refer toa difference between baseline BCVA and BCVA after 3 injections (r=-0.27, p<0.01)and to the difference between baseline BCVA and final BCVA (r=0.254; p<0.01).

Influence of patient's sex on changes in BCVA.

In the analyzed group of 90 patients, there were 50 women and 40 men. The conducted statistics (U Mann Whitney and Wilcoxon) showed that BCVA differences (between final and initial BCVA) are not significantly different in the group of women and men at any stage of therapy (Z=-1,878, p<0,060).
Adverse events after intravitreal aflibercept injections:In the studied group of 90 patients each patient received 7 injections of aflibercept.In the course of anti-VEGF therapy, the following local adverse reactions after anti-VEGF injections were observed:1 subconjunctival bleeding that has been spontaneously absorbed after several weeks, 2 eyes - short-term slight increase in intraocular pressure, disappearing after1 h after administration of anti-VEGF injection, 5 eyes - slight swelling of the cornea after administration of a 5% solution of iodine povidone to the conjunctival sac during surgery in the O.R., 45 eyes - reddening at the puncture site with a feeling discomfort after anti-VEGF injection . None of the patients in the study group was diagnosed with endophtalmitis.In the studied group no cardiovascular incidents in the form of myocardial infarction, no cerebrovascular or other serious incidents have occurred in the 12-month period of observation during therapy with intravitreal aflibecerpt injections.

Discussion

Clinical trials have confirmed the high efficacy and safety of both registered medicine in the treatment of exudative AMD (aflibercept and ranibizumab). The intensity of therapy in the first year of treatment is of particular importance, which confirm the results of randomised clinical trials as well as real-life observations assessing the actual daily clinical practice. [38] Results of treatment of patients in analyzed group in the Prof. K. Gibi ski University Clinical Centre Medical University of Silesia in Katowice, are consistent with the results of clinical studies and confirm the efficacy and safety of aflibercept therapy in the first year of nAMD treatment. In the studied group of 90 patients, after first year of treatment with aflibercept a statistically significant improvement of mean BCVA was observed. The patients gained +2,47 letters (Z=-1,989; p<0,05) after 3 months and +9,29 letters (Z=-6,812, p<0,001) in ETDRS scale after 52 weeks of treatment. BCVA improvement was observed in 66 patients, stabilization in 19 patients and deterioration in 5 patients. The results in the studied group were similar to those obtained in large clinical studies VIEW 1 and VIEW 2. In the combined analysis of the VIEW 1 and VIEW 2 studies an average BCVA improvement of 8.3-9.3 letters after 52 weeks and of 6.6-7.9 letters after 96 weeks of observation was achieved. [39] It is important to note that the improvement in the best corrected visual acuity in the study group was dependent on the baseline BCVA. The analysis of Pearson's correlation showed statistically significant negative relationship between BCVA before therapy and improvement of the BCVA one year after aflibercept treatment. Patients with lower baseline BCVA achieved a greater improvement in the best corrected visual acuity BCVA than patients with a higher initial BCVA who have

achieved lower improvement in the number of letters in the ETDRS scale. The results of these observations are consistent with the reports from the literature. The initial BCVA is one of the most important prognostic factors in response to anti-VEGF therapy and final improvement of the best corrected visual acuity. [40] It is therefore so essential to recognise the disease and implement the treatment at the earliest possible stage of the disease in order to obtain the best possible morphological and functional results.

At the same time the statistical significant reduction of CRT in OCT was observed. The most statistically significant ($Z=-6.903$; $p<0.001$) thickness reduction of the central retina occurred after the saturation phase, i.e. after the first 3 injections of aflibercept. Further injections (between 3 and 7 injections) led to a slight decline in the thickness of the retina and to support the morphological effect obtained, but without statistically significant differences ($Z=-0.766$; $p>0.05$). These observations are consistent with literature data that indicate that the highest CRT reduction occurs after administration of the first three injections and systematic injection of the anti-VEGF leads to an improvement in BCVA, also at a later stage of treatment when the morphology of the retina in the OCT image is not changing significantly. [36-37, 41-43]

In the study group, age correlated statistically significantly with the BCVA changes ($r=0,254$; $p<0,01$). However, this is a weak, negative correlation that could suggest that younger patients could be expected to have better performance in improving BCVA. In the literature, there are similar examples of reports on the correlation between age and improved visual acuity. In the analysis of groups in the MARINA study, it was shown that in the group of patients with a mean age lower by 13.7 years in comparison to the older age group, the improvement in visual acuity was on average 5 letters higher in the younger group than in the older patients. [44] Similarly analysis in the ANCHOR clinical trial showed that younger patients achieved a higher improvement best corrected visual acuity compared to older patients. [45] In the light of these data, AMD screening from the age of 45 is important due to possible better prognosis of improvement in visual acuity in early treatment implementation.

Another factor studied was the influence of the neovascular membrane type diagnosed in fluorescein angiography on the BCVA results. The analysis showed that there were no significant statistical differences in the BCVA range between groups with mixed, classical and occult type of neovascular membrane. In the literature, we find reports that the type of neovascular membrane influences the prognosis after anti-VEGF therapy, classical and partially classical membranes (mixed) usually have better prognosis than occult ones. Presence of fibrovascular PED (pigment epithelial detachment) with the accompanying occult CNV form is characterized by a worse response to anti-VEGF therapy, which can have a connection to the difficult RPE penetration of aflibercept from the vitreous to retina and choroid. [46-47]Other authors point to the fact that the size of the CNV lesion is more important in terms of a BCVA prognosis after anti-VEGF therapy than the type of CNV itself. Smaller neovascular membranes have better prognosis than big CNV lesions. [48]

A further clinical aspect assessed in this paper was the division of patients into pseudophakic and phakic in the context of BCVA post-treatment results after aflibercept intravitreal injections . In the study group 73 patients were phakic, and 17 patients were pseudophakic. The analysis showed that there were no statistically significant differences in the BCVA and CRT range between phakic and pseudophakic groups. The obtained results are consistent with the literature data. There are few reports in the research literature investigating influence of lens status on the results of anti-VEGF treatment in nAMD. All of them concern ranibizumab and confirm that there are no differences in the degree of BCVA improvement achieved after treatment as well as in reduction of central retina thickness between phakic and pseudophakic patients. [49-52]

Conclusions

The analysis showed high effectiveness and safety of aflibercept therapy after the first year of treatment in patients with age-related macular degeneration. Aflibercept intravitreal therapy provided satisfactory functional and anatomical effects, which translated into statistically significant improvement of the best corrected visual acuity and statistically significant reduction of the mean central thickness of retina after one year of therapy. The initial BCVA was one of the most important prognostic factors in response to anti-VEGF therapy and final improvement of the best corrected visual acuity. The intravitreal therapy with aflibercept is effective and safe for treating patients with wet AMD in routine daily practice. The obtained results proves the efficacy of treatment with aflibercept in patients with wet AMD and indicate the importance of early diagnose and treatment implementation to obtain the best functional and morphological results.

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