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Treatment of age related macular degeneration (AMD) currently and in the past

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Abstract:

Age-related macular degeneration (AMD) is a disease that blurs the sharp, central vision you need for "straight-ahead" activities such as reading, sewing, and driving. AMD affects the macula, the part of the eye that allows you to see fine detail. AMD causes no pain.

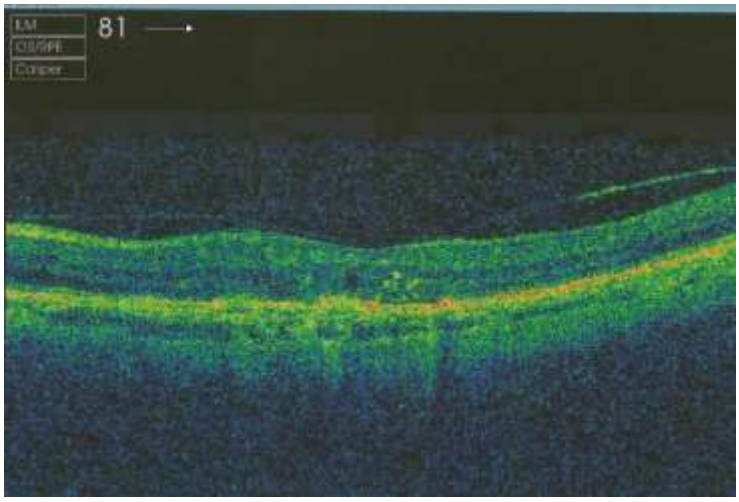
AMD is an irreparable disorder, which mostly occurs among people after 50. Nowadays the pathogenesis of AMD is still not entirely clarified, however, this disorder has multifactor background, which include interactions between genetic and environmental factors. AMD is divided into two forms: exudative ("wet") and nonexudative ("dry"). The treatment of age-related macular degeneration depends on the stage of the disease progression. One of the first methods of treatment of exudative AMD was laser photocoagulation with argon laser. Currently, this kind of treatment is used in certain cases of neovascularization in extrafoveal

area. Next elderly method of therapy of AMD was a photodynamic therapy (PDT) at year 2000. The treatment consist in intravenous injection of verteporfin and a laser at the same time. At 2002 was in use transpupillary thermotherapy (TTT).

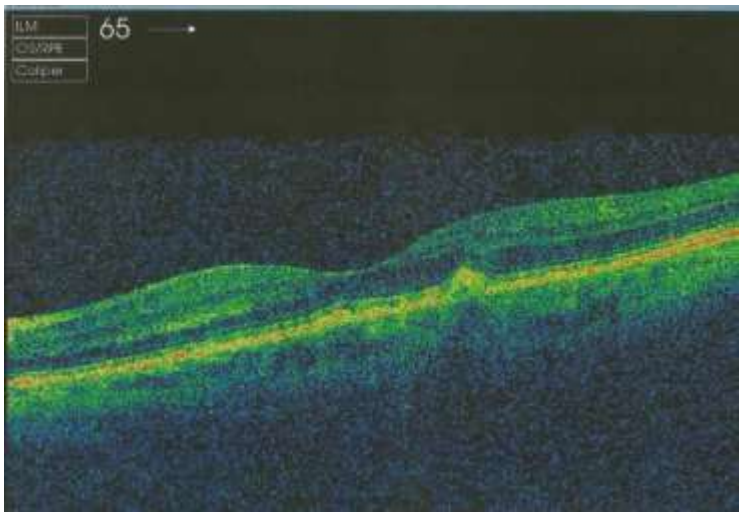
Last few years for treatment AMD is used antagonist of vascular endothelial growth factor (VEGF). We distinguish: pegatanib, ranibizumab, bevacizumab and aflibercept. Nowadays all of available methods do not eliminate causes of that disorder and in this connection currently treatment is still symptomatic. Apart from every mentioned method above, nutritional therapy is also essential and it decrease the risk of progression of AMD. The diet should contain products full of vitamin C,E, beta carotene, zinc and cooper.

Introduction:

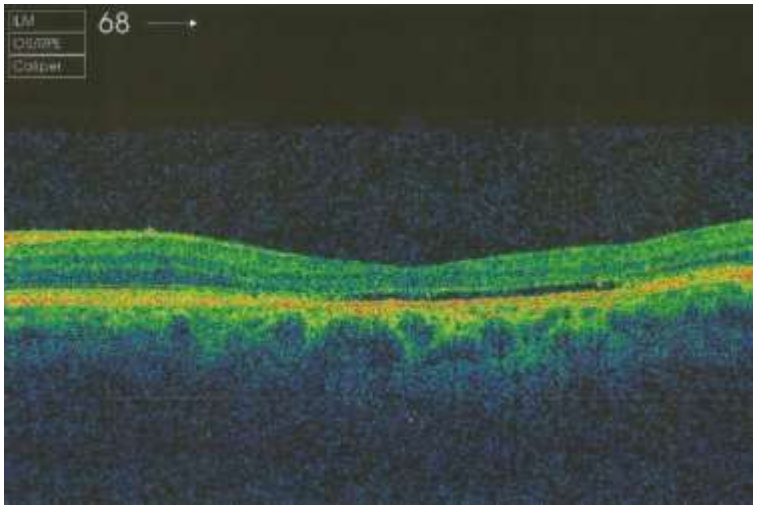
Age-related macular degeneration (AMD) is an irreparable disorder, which mostly occurs after age 50 (above 60 years old). The disease can unavoidably leads to serious visions loss, even to absolute blindness [1,2,3]. Nowadays the pathogenesis of AMD is still not entirely clarified, however this disorder has multifactor background, which include interactions between genetic and environmental factors [4]. According to past nomenclature AMD is divided into three groups, which contain early nonexudative ("dry"), late nonexudative ("athropic") and exudative/neovascular ("wet") [5]. Dry form is the most frequent and it occurs among more than 90% cases with AMD [6]. Patients with non-exudative type have small to no central vision loss [5].This group contains pigmentary modifications, drusen, basal laminar and linear deposits [7]. In the case of wet form of AMD, which is known as a less frequent one (10% of patients with AMD), it is known that the legal blindness is caused by choroidal neovascularization, tinal angiomatous proliferation or retinal pigment epithelial detachment [8, 9, 10]. Nowadays, there are little changes in nomenclature, which distinguish early AMD, in which the neovascularization is absent and late AMD, in which neovascularization is present[11]. That division has a purpose to show that there is a consistency between each forms of AMD and the early stadium can become more advanced like geographic atrophy and exudative form [12].



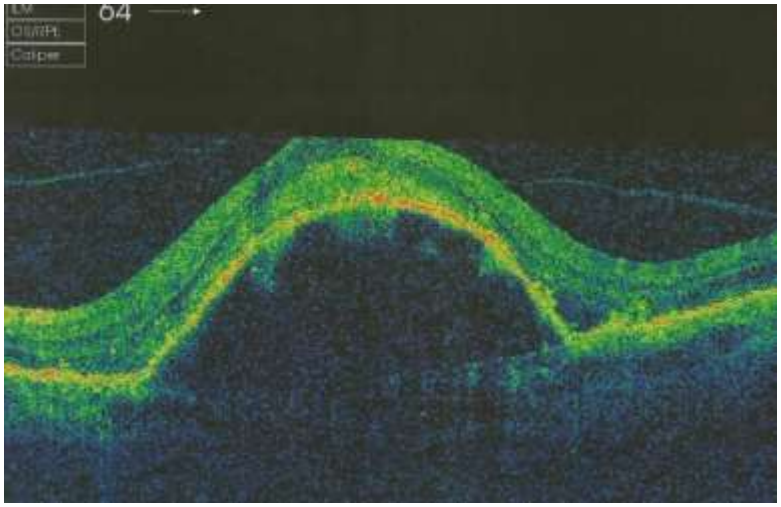
AMD, RPE disorder



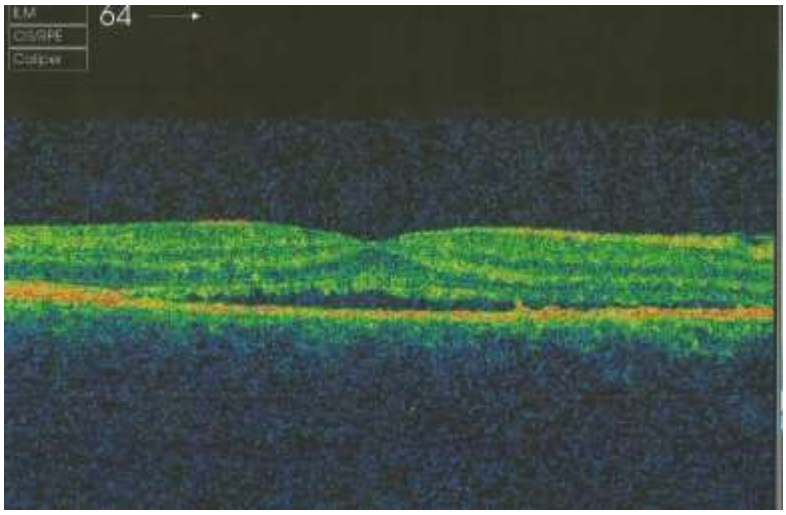
OCT- AMD dry form, drusen



OCT- AMD wet form, visible fluid



OCT- AMD wet form with pigment epithelium detachment (PED)



OCT- AMD wet form with retinal detachment

Aim of study:

The aim of study is to analyze ways of treatment of age-related macular degeneration through years.

Material and Methods:

The data comes from database PubMed, Google Scholar and own photos.

Results:

The treatment of age-related macular degeneration depends on the stage of the disease progression [13]. In the case of early stadium, the prevention is a cure and it contains nutritional therapy, full of antioxidants which are essential to improve function of cells of

macula [14]. One of the first methods of treatment of exudative AMD was laser photocoagulation with argon or another laser, which functioned within visible spectrum[15]. Effectiveness of this kind of treatment was visible in extrafoveal lesions[16,17]. Nonetheless, the outcome in parafoveal lesions was less spectacular[18,19]. Unfortunately, this method is connected with a high recurrence rate of disease, mainly severe visual loss [20]. According to data relapse of disorder with visual forfeiture took place between early post-treatment period and 5 years later. Nowadays green argon laser (514nm) has been substituted by Green 532-nm frequency-doubled Nd-YAG [21]. Currently, this kind of treatment is used in certain cases of neovascularization in extrafoveal area. Next elderly method of therapy of AMD is a photodynamic therapy (PDT). The treatment consist in intravenous injection of verteporfin, which is activated in neovascularization areas by a laser with small energy and wavelength 689 nm. This process leads to destruction and occlusion of pathological vessels by reactive oxygen species [15]. It is known, that in some cases PDT has to be repeated to achieve therapeutic success, although long-term response is variable with a different time of recurrence of disease in spite of several retreatments [21]. According to data 29% of patient who gained PDT therapy for occult sub foveal choroidal neovascularization (CNV) lost 6 or more lines of vision and 55% of patients lost 3 or more lines of vision after 2 years [22]. Nowadays guidelines and data define that photodynamic therapy is dedicated to AMD with predominantly classic CNV [23,24,25]. Surveys shows mixed therapy with a PTD and intravitreal anti-VEGF can improve vision in cases in which monotherapy with anti-VEGF was insufficient [26]. It is known that both elderly forms of treatment like photocoagulation and photodynamic therapy can be also used among patients, who cannot have intravitreal injections [21].

The use of antiangiogenic factors and antagonist of vascular endothelial growth factor (VEGF) as a specific treatment of diseases was mentioned in the literature more than 40 years ago [27]. Pegaptanib is a antiangiogenic 28-base ribonucleic acid aptamer, which has an ability to bind and block VEGF, especially 165-amino-acid isoforms [28]. There were clinical trials performed, in which the research group was divided into 3 group, with different dose of pegaptanib (0.3, 1.0, 3.0 mg) and control group was given usual treatment with photodynamic therapy. The risk of serious loss of visual acuity was 10% in research group and 22% in control cohort. This therapy gives statistically significant results among patients with neovascular age-related degeneration [25]. It is known that increasing the dose of pegaptanib for more than 0.3 mg has no impact for improvement of visual acuity and stadium of disease [15]. Many surveys, performed on animal choroidal and retinal models, showed that rise up

of new vessels is inseparably bonded with VEGF [29,30]. Because of that fact anti-VEGF factors have started to be used in AMD therapy by intravitreal injections. Ranibizumab is one of the anti-VEGF monoclonal antibodies, which binds and inactivates all forms of VEGF [31]. Moreover, with its short intravitreal half time, good penetration to retina and fast systemic disposal, it is very safe and effective [32,33]. MARINA was one of the trial study, which was performed to compare effectiveness of ranibizumab (0.3 or 0.5 mg dose group) with sham group in 24-monthly therapy [33]. First results of a treatment by ranibizumab were seen quickly after 3 months, and the vision was stable till the end of the experiment. After this time, 90% of patient from "0,5mg group" kept stable vision without loss of more than 15 letters, while in control group was 53%[33]. Bevacizumab is recombined, humanized monoclonal antibody, which binds with all VEGF isoforms [15]. It is also registered as a anti-angiogenic therapy among patients with oncological diseases such as colorectal cancer [34]. Results of one meta-analysis, which compared ranibizumab with bevacizumab detected no significant difference in change in best correct visual acuity (BCVA) after one year of treatment of neovascular AMD [35]. There are also surveys, in which the combination of bevacizumab and triamcinolon was examined. This mix was detected as a more effective treatment improving BCVA than monotherapy with bevacizumab [36]. Another commonly used treatment is aflibercept, which is a recombinant protein containing extracellular parts of VEGF receptors 1 and 2. It has also great affinity to VEGF 165a [37]. In retrospective analysis comparing aflibercept and ranibizumab BCVA scores did not statistically diverge. The only one variation were anatomic results measured by optical coherence tomography (OCT), which were better among patients who received aflibercept [38].

The Comparison of AMD Treatments Trials (CATT) began in 2008 and was designed to compare the anti-VEGF drugs Avastin and Lucentis. VEGF is important in the growth and development of new blood vessels in normal and cancerous tissues. Avastin (bevacizumab) was approved by the Food and Drug Administration in 2004 for the treatment of metastatic colon cancer. Other drugs were later developed specifically to target blood vessels in the retina, with Lucentis (ranibizumab) coming to the market in 2006 and Eylea (aflibercept) in 2011. For treating AMD, the drugs are injected into the eye. Before Lucentis was available, many ophthalmologists began treating the disease with Avastin, which appeared to have similar benefits, at least in the short-term.

Scientists at the National Eye Institute (NEI), part of the National Institutes of Health, report that tiny tube-like protrusions called primary cilia on cells of the retinal pigment epithelium (RPE)—a layer of cells in the back of the eye—are essential for the survival of the retina's

light-sensing photoreceptors. The discovery has advanced efforts to make stem cell-derived RPE for transplantation into patients with geographic atrophy, otherwise known as dry age-related macular degeneration (AMD), a leading cause of blindness in the U.S. The study appears in the January 2 Cell Reports.

“We now have a better idea about how to generate and replace RPE cells, which appear to be among the first type of cells to stop working properly in AMD,” said the study’s lead investigator, Kapil Bharti, Ph.D., Stadtman investigator at the NEI. Bharti is leading the development of patient stem cell-derived RPE for an AMD clinical trial set to launch in 2018.

In a healthy eye, RPE cells nourish and support photoreceptors, the cells that convert light into electrical signals that travel to the brain via the optic nerve. RPE cells form a layer just behind the photoreceptors. In geographic atrophy, RPE cells die, which causes photoreceptors to degenerate, leading to vision loss.

Bharti and his colleagues are hoping to halt and reverse the progression of geographic atrophy by replacing diseased RPE with lab-made RPE. The approach involves using a patient’s blood cells to generate induced-pluripotent stem cells (iPSCs), cells capable of becoming any type of cell in the body. iPSCs are grown in the laboratory and then coaxed into becoming RPE for surgical implantation.(41)

Eating a healthy diet and getting exercise have been shown in earlier studies to protect against AMD, a leading cause of vision loss among people age 50 and older. Findings from this latest study, conducted by a team of investigators at the University of Wisconsin-Madison, suggest that genetic and lifestyle factors may contribute to AMD in a synergistic way. The findings were published online in the journal Ophthalmology.

Conclusion:

National Eye Institute looks ahead between 2010 and 2050, the estimated number of people with AMD will more than double from 2,1 million to 5,4 million.

Age-related macular degeneration is a disorder with still no - entirely discovered pathogenesis. Researchers all over the world are still searching for more modern and safer treatment. Nowadays all of available methods do not eliminate causes of that disorder and in this connection currently treatment is still symptomatic. Currently anti-VEGF factors are known as a treatment of AMD recommended to many types of this disease. Apart from every mentioned method above, nutritional therapy is also essential and it decrease the risk of progression of AMD. The diet should contain products full of vitamin C,E, beta-carotene,

zinc and copper [39]. Another surveys performed a few years later showed that also adding lutein and zeaxanthin can reduce the risk of progression for about 10 to 20 % [40].

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