

Issue 299

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This free weekly bulletin lists the latest published research articles on macular degeneration (MD) and some other macular diseases as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases.

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Drug treatment

Graefes Arch Clin Exp Ophthalmol. 2016 Sep 28. [Epub ahead of print]

Reduced-fluence verteporfin photodynamic therapy plus ranibizumab for choroidal neovascularization in pathologic myopia.

Rinaldi M, Semeraro F, Chiosi F, Russo A, Romano MR, Savastano MC, dell'Omo R, Costagliola C.

BACKGROUND: To demonstrate the efficacy of intravitreal ranibizumab (IVR) in combination with reduced-fluence photodynamic therapy (RF-PDT) in patients with choroidal neovascularization (CNV) secondary to pathologic myopia.

METHODS: Sixty patients affected by myopic CNV (mCNV) were randomized to receive either ranibizumab 0.5 mg monotherapy (RM; n = 20), standard fluence PDT (SF-PDT, n = 20) or RF-PDT combination therapy (n = 20). Subsequently, IVR was injected as needed. All patients were evaluated for 48 weeks.

RESULTS: Mean BCVA change at 48 weeks was + 0.2 and +15 letters with SF or RFPDT plus ranibizumab, respectively, compared with +16.8 letters with RM. At 48 weeks, mean central foveal thickness (CFT) decrease from baseline was $58 \pm 15 \mu\text{m}$, $91.4 \pm 43.8 \mu\text{m}$, and $85 \pm 41.5 \mu\text{m}$ for the verteporfin SF, RF and RM groups, respectively. Macular sensitivity improvement was + 0.4 db, + 1.9 dB and + 2.7 dB for the verteporfin SF, RF and RM groups, respectively.

CONCLUSIONS: Ranibizumab monotherapy or combined with RF-PDT improved BCVA and macular sensitivity in patients affected by mCNV, whereas CFT results were reduced. SF-PDT combination regimen mostly stabilized vision at 48 weeks. Among all groups, the RF-PDT seemed to reduce the number of ranibizumab retreatments.

PMID: 27680013

Int J Ophthalmol. 2016 Sep 18;9(9):1304-9.

Influence of CFH, HTRA1 and ARMS2 polymorphisms in the response to intravitreal ranibizumab treatment for wet age-related macular degeneration in a Spanish population.

Cruz-Gonzalez F, Cabrillo-Estevez L, Rivero-Gutierrez V, Sanchez-Jara A, De Juan-Marcos L, Gonzalez-Sarmiento R.

AIM: To determine whether gene polymorphisms of the major genetic risk loci for age-related macular degeneration (AMD): ARMS2 (rs10490923), the complement factor H (CFH) (rs1410996) and HTRA1 (rs11200638) influence the response to a treatment regimen with ranibizumab for exudative AMD.

METHODS: This study included 100 patients (100 eyes) with exudative AMD. Patients underwent a treatment with ranibizumab injections monthly during three months. Reinjections were made when the best

corrected visual acuity (BCVA) decrease five letters (ETDRS) or central subfield retinal thickness gained 100 µm in optical coherence tomography image. Genotypes (rs10490923, rs1410996 and rs11200638) were analyzed using TaqMan probes or polymerase chain reaction-restricted fragment length polymorphisms analysis.

RESULTS: There were no statistically significant differences in allelic distribution of CFH (rs1410996), ARMS2 (rs10490923) and HTRA1 (rs11200638) polymorphisms regarding to response to ranibizumab treatment.

CONCLUSION: Ranibizumab treatment response is not related to CFH (rs1410996), ARMS2 (rs10490923) and HTRA1 (rs11200638) polymorphisms.

PMID: 27672596 PMCID: PMC5028666

Curr Med Res Opin. 2016 Sep 29:1-7. [Epub ahead of print]

Intravitreal anti-VEGF drug use in industrialized nations: why are newly introduced medications causing us to inject more and not less?

Stewart MW.

PMID: 27684540

Other treatment & diagnosis

Retina. 2016 Sep 28. [Epub ahead of print]

VISUALIZING RETINAL PIGMENT EPITHELIUM PHENOTYPES IN THE TRANSITION TO ATROPHY IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

Zanzottera EC, Ach T, Huisinigh C, Messinger JD, Freund KB, Curcio CA.

PURPOSE: To enable future studies of retinal pigment epithelium (RPE) fate in the macular atrophy occurring in eyes with neovascular age-related macular degeneration (nvAMD), the authors determined how RPE morphology changes across the transition from health to atrophy in donor eyes with nvAMD.

METHOD: In RPE-Bruch membrane flat mounts of 5 nvAMD eyes, the terminations of organized RPE cytoskeleton and autofluorescent material were compared. In high-resolution histologic sections of 27 nvAMD eyes, RPE phenotypes were assessed at ±500 µm and ±100 µm from the descent of the external limiting membrane (ELM) toward the Bruch membrane. Thicknesses of RPE, basal laminar deposit (BLamD), and RPE + BLamD were determined. Shapes of the ELM descent were recorded.

RESULTS: Approaching the ELM descent, the percentage of different RPE phenotypes and the thickness of RPE, BLamD, and RPE + BLamD each stayed roughly constant. Compared with a separately described cohort of eyes with geographic atrophy, eyes with nvAMD were more likely to have RPE dysmorphia that did not worsen toward the atrophy border, thinner BLamD overall (3.25 ± 3.46 µm vs. 7.99 ± 7.49 µm for geographic atrophy), and a higher proportion of oblique ELM descents (47.9 vs. 31.9%).

CONCLUSION: The distribution of RPE phenotypes at the transition to macular atrophy in eyes with nvAMD differs from that in primary geographic atrophy, likely reflecting greater photoreceptor loss and the effects of exudation in nvAMD. This distribution, the shape of ELM descents, and thickness profiles may be useful metrics in clinical studies of macular atrophy using optical coherence tomography and fundus autofluorescence.

PMID: 27685678

Retina. 2016 Sep 28. [Epub ahead of print]

TOWARD QUANTITATIVE OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY: Visualizing Blood Flow Speeds in Ocular Pathology Using Variable Interscan Time Analysis.

Ploner SB, Moulton EM, Choi W, Waheed NK, Lee B, Novais EA, Cole ED, Potsaid B, Husvot L, Schottenhamml J, Maier A, Rosenfeld PJ, Duker JS, Hornegger J, Fujimoto JG.

PURPOSE: Currently available optical coherence tomography angiography systems provide information about blood flux but only limited information about blood flow speed. The authors develop a method for mapping the previously proposed variable interscan time analysis (VISTA) algorithm into a color display that encodes relative blood flow speed.

METHODS: Optical coherence tomography angiography was performed with a 1,050 nm, 400 kHz A-scan rate, swept source optical coherence tomography system using a 5 repeated B-scan protocol. Variable interscan time analysis was used to compute the optical coherence tomography angiography signal from B-scan pairs having 1.5 millisecond and 3.0 milliseconds interscan times. The resulting VISTA data were then mapped to a color space for display.

RESULTS: The authors evaluated the VISTA visualization algorithm in normal eyes (n = 2), nonproliferative diabetic retinopathy eyes (n = 6), proliferative diabetic retinopathy eyes (n = 3), geographic atrophy eyes (n = 4), and exudative age-related macular degeneration eyes (n = 2). All eyes showed blood flow speed variations, and all eyes with pathology showed abnormal blood flow speeds compared with controls.

CONCLUSION: The authors developed a novel method for mapping VISTA into a color display, allowing visualization of relative blood flow speeds. The method was found useful, in a small case series, for visualizing blood flow speeds in a variety of ocular diseases and serves as a step toward quantitative optical coherence tomography angiography.

PMID: 27685677

Retin Cases Brief Rep. 2016 Sep 28. [Epub ahead of print]

A CASE OF CONE DYSTROPHY ASSOCIATED WITH CHOROIDAL NEOVASCULARIZATION.

Gulkilik G, Erdur SK, Eliacik M, Odabasi M, Ozsutcu M, Demirci G, Kocabora MS.

PURPOSE: To report a case of choroidal neovascularization (CNV) in a patient with cone dystrophy (CD).

METHODS: Case report.

RESULTS: A 20-year-old woman presented with diminished vision in her right eye. Fundus examination showed perifoveal retinal pigment epithelial changes and retinal hemorrhage consistent with subretinal CNV in the right eye, and mild retinal pigment epithelial changes with a dull foveal reflex in the left eye. Optical coherence tomography analysis and fundus fluorescein angiography also confirmed the subfoveal CNV in the right eye. Electroretinography showed decreased amplitudes in photopic and 30-Hz flicker tests in both eyes, which confirmed cone dystrophy. A single intravitreal ranibizumab injection resolved the edema and stabilized the CNV during the follow-up of 6 months.

CONCLUSION: Cone dystrophy is an inherited ocular disorder characterized by loss of cone photoreceptors. Association of CNV has been reported in patients with fundus flavimaculatus, best dystrophy, gyrate atrophy, choroideremia, retinitis pigmentosa, adult-onset foveomacular vitelliform dystrophy, Sorsby macular dystrophy, Bietti crystalline dystrophy, and myotonic dystrophy-related macular dystrophy. We report a case of a patient with CD in whom CNV developed in one eye and responded to a single ranibizumab injection.

PMID: 27685498

J Vis Exp. 2016 Sep 13;(115). doi: 10.3791/53927.

A Step by Step Protocol for Subretinal Surgery in Rabbits.

Al-Nawaiseh S, Thieltges F, Liu Z, Strack C, Brinken R, Braun N, Wolschendorf M, Maminishkis A, Eter N, Stanzel BV.

Abstract: Age related macular degeneration (AMD), retinitis pigmentosa, and other RPE related diseases are the most common causes for irreversible loss of vision in adults in industrially developed countries. RPE transplantation appears to be a promising therapy, as it may replace dysfunctional RPE, restore its function, and thereby vision. Here we describe a method for transplanting a cultured RPE monolayer on a scaffold into the subretinal space (SRS) of rabbits. After vitrectomy xenotransplants were delivered into the SRS using a custom made shooter consisting of a 20-gauge metallic nozzle with a polytetrafluoroethylene (PTFE) coated plunger. The current technique evolved in over 150 rabbit surgeries over 6 years. Post-operative follow-up can be obtained using non-invasive and repetitive in vivo imaging such as spectral domain optical coherence tomography (SD-OCT) followed by perfusion-fixed histology. The method has well-defined steps for easy learning and high success rate. Rabbits are considered a large eye animal model useful in preclinical studies for clinical translation. In this context rabbits are a cost-efficient and perhaps convenient alternative to other large eye animal models.

PMID: 27684952

Medicine (Baltimore). 2016 Sep;95(39):e4978.

Cross-sectional pupillographic evaluation of relative afferent pupillary defect in age-related macular degeneration.

Takayama K1, Ito Y, Kaneko H, Nagasaka Y, Tsunekawa T, Sugita T, Terasaki H.

Abstract: To evaluate, using pupillography, the difference between eyes affected by age-related macular degeneration and their contralateral normal eyes with regard to the mean relative afferent pupillary defect (RAPD) score. Also, to ascertain any correlations between this difference in RAPD score and differences in visual acuity or age-related macular degeneration (AMD) dimensions. Measurements were made using the RAPDx pupillographer (Konan Medical, Nishinomiya, Japan), which analyzes pupil response to light stimulation. Both best corrected visual acuity (converted to logMAR) and greatest linear dimension (GLD; calculated on the basis of fluorescence angiography images) were measured. The correlations between RAPD difference and logMAR difference, and GLD difference were then analyzed. The study included 32 patients (18 men, 14 women; mean age = 74.8±9.7 years) who had AMD in 1 eye and a normal fundus in the contralateral eye. Mean resting pupil diameter, mean latency onset of constriction, mean velocity of constriction, and recovery were not significantly different in AMD eyes compared with normal eyes. The mean amplitude of constriction was smaller ($P = 0.028$), and the mean latency of maximum constriction was shorter ($P = 0.0013$) in AMD eyes than in normal eyes. Regarding RAPD scores, there was a significant correlation between visual acuity difference and RAPD score differences of both amplitude ($P < 0.001$, $r = 0.53$) and latency ($P = 0.034$, $r = 0.33$). GLD difference was also significantly correlated with differences in both amplitude ($P = 0.021$, $r = 0.36$) and latency ($P = 0.033$, $r = 0.33$) scores. RAPD outcomes were correlated with visual acuity and AMD dimension. Automated pupillography may be a useful tool in monitoring the progression of AMD and assessing changes in retinal function that result from novel interventions.

PMID: 27684848

Pathogenesis

Oxid Med Cell Longev. 2016;2016:6819736. Epub 2016 Sep 5.

Melatonin in Retinal Physiology and Pathology: The Case of Age-Related Macular Degeneration.

Blasiak J, Reiter RJ, Kaarniranta K.

Abstract: Melatonin, an indoleamine, is synthesized mainly in the pineal gland in a circadian fashion, but it is produced in many other organs, including the retina, which seems to be especially important as the eye is a primary recipient of circadian signals. Melatonin displays strong antioxidative properties, which predispose it to play a protective role in many human pathologies associated with oxidative stress, including premature aging and degenerative disease. Therefore, melatonin may play a role in age-related macular degeneration (AMD), a disease affecting photoreceptors, and retinal pigment epithelium (RPE) with an established role of oxidative stress in its pathogenesis. Several studies have shown that melatonin could exert the protective effect against damage to RPE cells evoked by reactive oxygen species (ROS), but it has also been reported to increase ROS-induced damage to photoreceptors and RPE. Melatonin behaves like synthetic mitochondria-targeted antioxidants, which concentrate in mitochondria at relatively high levels; thus, melatonin may prevent mitochondrial damage in AMD. The retina contains telomerase, an enzyme implicated in maintaining the length of telomeres, and oxidative stress inhibits telomere synthesis, while melatonin overcomes this effect. These features support considering melatonin as a preventive and therapeutic agent in the treatment of AMD.

PMID: 27688828

Epidemiology

Curr Opin Ophthalmol. 2016 Sep 28. [Epub ahead of print]

Cataract surgery and age-related macular degeneration.

Ehmann DS, Ho AC.

PURPOSE OF REVIEW: The following review describes the recent evidence regarding the effect of cataract surgery on age-related macular degeneration (AMD).

RECENT FINDINGS: For patients with both visually significant cataracts and AMD, recent evidence supports the role of cataract surgery with reports demonstrating improved visual acuity, absence of significant disease progression, and improved quality of life.

SUMMARY: Recent evidence does not find cataract surgery to cause or worsen AMD.

PMID: 27684293

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