

Issue 57

Tuesday November 29 , 2011

This free weekly bulletin lists the latest published research articles on macular degeneration (MD) as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term "macular degeneration".

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Drug treatment

Invest Ophthalmol Vis Sci. 2011 Nov 22. [Epub ahead of print]

Retinal Venular Caliber Predicts Visual Outcome Following Intra-vitreous Ranibizumab Injection Treatments For Neovascular AMD.

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Objective: To examine whether baseline retinal vascular caliber predicts visual response to intravitreal ranibizumab injections in patients with neovascular age-related macular degeneration (AMD).

Methods: In this prospective cohort study, patients with neovascular AMD received three monthly intravitreal injections of ranibizumab, followed by pro re nata dosing up to one year. Retinal vascular caliber was measured from digital fundus photographs at baseline and summarized as central retinal artery equivalent (CRAE) and venular equivalent (CRVE), representing average caliber of arterioles and venules, respectively. Visual outcome at 12 months was assessed and the relation to baseline retinal vascular caliber was determined.

Results: A total of 88 eyes were analyzed at baseline. After accounting for age, gender, size of choroidal neovascularization (CNV) and number of injections, patients who deteriorated in visual acuity at 12 months had significantly larger baseline CRVE, 243.10µm (95%CI, 227.01, 259.19), compared to those who were stable, 214.30µm (95%CI 205.79, 222.81) and those who improved, 215.26µm (95%CI 204.69, 225.84), $p=0.007$. Baseline CRAE did not differ significantly eyes whose vision deteriorated, 150.12µm (95%CI 140.67, 159.57), compared to those remaining stable, 143.64µm (95%CI 138.64, 148.63), or gaining vision 142.92µm (95%CI 136.71, 149.13), $p=0.69$.

Conclusion: In eyes with neovascular AMD treated with intravitreal ranibizumab, larger baseline retinal venular caliber was significantly associated with a poorer response to treatment, possibly reflecting increased disease severity.

PMID: 22110075 [PubMed - as supplied by publisher]

Expert Rev Clin Pharmacol. 2010 Nov;3(6):747-52.

Bevacizumab for neovascular age-related macular degeneration (ABC trial): multicenter randomized

double-masked study.

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Abstract

Evaluation of: Tufail A, Patel PJ, Egan C et al.; ABC Trial Investigators. Bevacizumab for neovascular age related macular degeneration (ABC trial): multicentre randomised double masked study. BMJ 340, c2459 (2010). The ABC trial is the first multicenter, randomized clinical trial that addresses the safety and efficacy of bevacizumab (Avastin®), Genentech, Inc., CA, USA) in the treatment of neovascular age-related macular degeneration. The trial showed that an initial loading dose of three intravitreal injections of Avastin 1.25 mg at 6-week intervals, followed by a 6-weekly variable retreatment regimen, according to strict functional and anatomic criteria for up to 1 year, is safe and effective. The results are in line with those reported previously in the pivotal ranibizumab (Lucentis®, Genentech, Inc.) trials following monthly intravitreal injections. The trial also exemplifies the paradigm shift in primary end point selection and patient expectation that the arrival of anti-VEGF agents, such as Lucentis and Avastin, has allowed for. Instead of visual stabilization and retardation of visual loss, patients and physicians now expect visual improvement following treatment. Such expectation was almost unrealistic prior to the availability of these agents.

PMID: 22111778 [PubMed - in process]

Retina. 2011 Nov 16. [Epub ahead of print]

PROGNOSTIC FACTORS FOR VISUAL OUTCOME AFTER INTRAVITREAL ANTI-VEGF INJECTION FOR NAIVE MYOPIC CHOROIDAL NEOVASCULARIZATION.

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PURPOSE: The aim of this study was to evaluate the prognostic factors of visual outcome after intravitreal anti-vascular endothelial growth factor injection in patients with myopic choroidal neovascularization (CNV).

METHODS: Forty eyes of 40 consecutive patients with myopic CNV who had received intravitreal ranibizumab or bevacizumab injections were retrospectively reviewed. Baseline visual acuity, presence of lacquer crack, dark rim, peripapillary choroidal atrophy size, and location of myopic CNV were evaluated using fluorescein angiography and indocyanine green angiography.

RESULTS: The logarithm of the minimum angle of resolution best-corrected visual acuity (BCVA) at 12 months after treatment was 0.23 ± 0.28 , and there was a significant improvement compared with the baseline BCVA ($P = 0.001$). After multiple linear regression analysis, baseline BCVA, presence of lacquer crack extending the fovea, and peripapillary choroidal atrophy size were the factors that significantly correlated with BCVA at 12 months ($P = 0.001$, $P = 0.04$, and $P = 0.04$). For mean change in BCVA over 12 months, there were also significant correlations with baseline BCVA, lacquer crack extension to the fovea, and peripapillary choroidal atrophy size ($P = 0.001$, $P = 0.03$, and $P = 0.03$). The mean number of anti-vascular endothelial growth factor injections was 2.8 ± 2.0 over 12 months. Complete resolution of myopic CNV was noted in 22 eyes (55.0%) after initial first injection, and no additional treatment was required in 12 eyes (30%).

CONCLUSION: Better baseline BCVA, lacquer crack extension to the fovea, and peripapillary atrophy were negative prognostic factors of visual acuity improvement, and there was quite a promising result of anti-vascular endothelial growth factor treatment in patients with myopic CNV.

PMID: 22105498 [PubMed - as supplied by publisher]

Other treatment & diagnosis

J Cataract Refract Surg. 2011 Dec;37(12):2115-9.

Effects of blue light-filtering intraocular lenses on the macula, contrast sensitivity, and color vision after a long-term follow-up.

Kara-Junior N, Espindola RF, Gomes BA, Ventura B, Smadja D, Santhiago MR.

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PURPOSE: To evaluate the possible side effects and potential protection 5 years after implantation of an intraocular lens (IOL) with a blue-light filter (yellow tinted).

SETTING: Ophthalmology Department, University of São Paulo, São Paulo, Brazil.

DESIGN: Prospective randomized clinical study.

METHODS: Patients with bilateral visually significant cataract randomly received an ultraviolet (UV) and blue light-filtering IOL (Acrysof Natural SN60AT) in 1 eye and an acrylic UV light-filtering only IOL (Acrysof SA60AT) in the fellow eye. The primary outcome measures were contrast sensitivity, color vision, and macular findings 5 years after surgery.

RESULTS: The study enrolled 60 eyes of 30 patients. There were no significant clinical or optical coherence tomography findings in terms of age-related macular degeneration in any eye. There were no statistically significant differences in central macular thickness between the 2 IOL groups ($P=.712$). There were also no significant between-group differences under photopic or scotopic conditions at any spatial frequency studied. No statistically significant differences in the color discrimination test were found between the 2 IOL groups ($P=.674$).

CONCLUSIONS: After 5 years, there were no significant differences in color perception, scotopic contrast sensitivity, or photopic contrast sensitivity between the blue light-filtering (yellow-tinted) IOL and the IOL with a UV-light filter only (untinted). The potential advantage of the tinted IOL in providing protection to macular cells remains unclear.

PMID: 22108107 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2011 Nov 22. [Epub ahead of print]

Blue Light versus Green Light Autofluorescence: Lesion Size of Areas with Geographic Atrophy.

Wolf-Schnurrbusch UE, Wittwer VV, Ghanem R, Niederhaeuser M, Enzmann V, Framme C, Wolf S.

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Introduction: Blue light fundus autofluorescence (FAF) imaging is currently widely used for assessing dry age-related macular degeneration (ARMD). However, at this wavelength the fovea appears as circular zone of marked hypofluorescence due to the absorption of macular pigment (MP). This dark spot could be misinterpreted as atrophic area and could lead to difficulties in identifying small central changes. The aim of the study was to analyze differences in image quality, FAF patterns, and lesion size of using conventional blue ($\lambda(1)=488$ nm) and green light FAF ($\lambda(2)=514$ nm).

Material and Methods: Patients older than 50 years with central areas of geographic atrophy (GA) secondary to ARMD were enrolled. Images were recorded with a modified confocal scanning laser ophthalmoscopy (cSLO). Image quality and patterns were analyzed. The quantification of the GA was

performed with a customized analysis imaging software.

Results: In total 95 eyes were included. Borders of the central atrophic patches and boundaries of preserved foveal island were better identified in 514 nm images. In both excitation wavelengths the signal-to-noise ratio was sufficient for the identification of FAF pattern. We found significant differences in the size of the GA areas detected in the 488 nm and 514 nm wavelength images ($4.29 \pm 3.76 \text{ mm}^2$ vs. $3.80 \pm 3.68 \text{ mm}^2$; $p < 0.001$).

Conclusion: The green light FAF images (514 nm) are superior for an accurate analysis of central small central pathologic changes and for the determination of the central GA lesion size. Using only blue light FAF could lead to an over-interpretation of the size of atrophic patches and the center involvement because it suggests the presence of atrophy in the fovea.

PMID: 22110076 [PubMed - as supplied by publisher]

Hippokratia. 2011 Apr;15(2):103-108.

Reading performance and central field loss.

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Abstract

Age-related macular degeneration is a major cause of blindness in Europe and the U.S. and a leading cause of significant loss of visual acuity in elderly patients. Reading is a key visual task in everyday living involving a synthesis of a number of different motor, sensory and cognitive functions. When the centre of a reader's visual field is obscured, reading speed declines and oculomotor pattern differs, compared to normal reading. Improvement in the generation of visual stimuli using computer-generated images and projection/display systems as well as advances in eye movement recording techniques, including infrared pupil tracking and magnetic search coils, have contributed greatly to our understanding of these sensorimotor abnormalities. The developed reading strategies have been thoroughly investigated in individuals with central field loss either induced artificially or related to eye pathology. The following review aims at presenting the contemporary literature regarding the sensory and oculomotor deficits in reading ability, resulting from central field loss and should contribute to a greater understanding of the functional visual deficit caused by this visual impairment.

PMID: 22110289 [PubMed - as supplied by publisher] PMCID: PMC3209671

J Biomed Opt. 2011 Nov;16(11):116016.

Retinal image restoration by means of blind deconvolution.

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Abstract

Retinal imaging plays a key role in the diagnosis and management of ophthalmologic disorders, such as diabetic retinopathy, glaucoma, and age-related macular degeneration. Because of the acquisition process,

retinal images often suffer from blurring and uneven illumination. This problem may seriously affect disease diagnosis and progression assessment. Here we present a method for color retinal image restoration by means of multichannel blind deconvolution. The method is applied to a pair of retinal images acquired within a lapse of time, ranging from several minutes to months. It consists of a series of preprocessing steps to adjust the images so they comply with the considered degradation model, followed by the estimation of the point-spread function and, ultimately, image deconvolution. The preprocessing is mainly composed of image registration, uneven illumination compensation, and segmentation of areas with structural changes. In addition, we have developed a procedure for the detection and visualization of structural changes. This enables the identification of subtle developments in the retina not caused by variation in illumination or blur. The method was tested on synthetic and real images. Encouraging experimental results show that the method is capable of significant restoration of degraded retinal images.

PMID: 22112121 [PubMed - as supplied by publisher]

Pathogenesis

Acta Ophthalmol. 2011 Nov 23. doi: 10.1111/j.1755-3768.2011.02179.x. [Epub ahead of print]

Molecular mechanisms of retinal pigment epithelium damage and development of age-related macular degeneration.

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Abstract

Age-related macular degeneration (AMD) is attributed to a complex interaction of genetic and environmental factors. It is characterized by degeneration involving the retinal photoreceptors, retinal pigment epithelium (RPE) and Bruch's membrane, as well as alterations in choroidal capillaries. AMD pathogenesis is strongly associated with chronic oxidative stress and inflammation that ultimately lead to protein damage, aggregation and degeneration of RPE. Specific degenerative findings for AMD are accumulation of intracellular lysosomal lipofuscin and extracellular drusens. In this review, we discuss thoroughly RPE-derived mechanisms in AMD pathology.

PMID: 22112056 [PubMed - as supplied by publisher]

Retina. 2011 Nov 16. [Epub ahead of print]

Influence of Vitreomacular Adhesion on the Development of Exudative Age-Related Macular Degeneration 4-Year Results of a Longitudinal Study.

Waldstein SM, Sponer U, Simader C, Sacu S, Schmidt-Erfurth U.

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PURPOSE: To investigate the influence of vitreomacular adhesion (VMA) on development of choroidal neovascularization (CNV) in eyes with age-related macular degeneration.

METHODS: In a prospective study, patients with Age-Related Eye Disease Study Category IV age-related

macular degeneration underwent standardized examinations, including optical coherence tomography and fluorescein angiography every 3 months for 4 years. Vitreomacular adhesion was evaluated using time- and spectral-domain optical coherence tomography. Development of CNV was detected using fluorescein angiography and optical coherence tomography. Incidences of CNV were compared concerning the presence or absence of VMA.

RESULTS: Forty-nine patients were available for follow-up according to protocol. Vitreomacular adhesion was present at baseline in 18% (9 of 49) and absent in 82% (40 of 49) of patients. Thirty-seven percent of patients (18 of 49) developed exudative changes during the observation period. In patients with preexisting VMA, de novo development of CNV occurred in 33% (3 of 9). In patients without VMA, 38% developed CNV (15 of 40). Mean interval from baseline to disease progression was 20 ± 19 months in patients with VMA and 22 ± 13 months in patients without VMA. There was no significant difference between the groups regarding rate of CNV development or time to disease progression ($P = 0.64$).

CONCLUSION: No significant influence of VMA on the development of exudative age-related macular degeneration could be found during a 4-year prospective observation of a high-risk cohort.

PMID: 22105497 [PubMed - as supplied by publisher]

Am J Pathol. 2011 Nov 19. [Epub ahead of print]

A Rat Model for Studying the Biological Effects of Circulating LDL in the Choriocapillaris-BrM-RPE Complex.

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Abstract

Retention of apolipoprotein B-containing lipoproteins in Bruch's membrane (BrM) is believed important in early age-related macular degeneration (AMD). The origin of the lipoproteins in BrM is a hot topic in AMD research. Some studies hypothesize an intraocular origin. BrM is in direct contact to the choriocapillaris; a plasma origin has also been suggested for the low-density lipoprotein (LDL) particles. We developed an animal model to study the biological effects of circulating LDL on the retina. After injection of LDL for 7 days, our results showed evidence of circulating apolipoprotein B100 retention in BrM and showed induction of early AMD-like alterations in the rat retina, such as thickening of BrM, photoreceptor TUNEL-positive cells, and inflammatory cell infiltration. In vitro assays showed that oxidized LDL (ox-LDL) treatment decreased ARPE-19 cell viability in a dose-dependent manner and that 10 mg/L ox-LDL induced marked apoptosis. The ratio of matrix metalloproteinase-2 to tissue inhibitors of metalloproteinase-3 was dysregulated after LDL and ox-LDL treatment in ARPE-19 cells, which can produce profound changes in the extracellular matrix, including thickening of and deposit formation in BrM. The observation that circulating LDL may be a significant, but not complete, origin of the lipoprotein in BrM suggests that these findings can be readily exploited for the development of new model systems and the future benefit of patients with AMD.

PMID: 22107828 [PubMed - as supplied by publisher]

Epidemiology

Biomed Environ Sci. 2011 Oct;24(5):506-11.

Risk Factors for Age-Related Macular Degeneration in Elderly Chinese population in Shenyang of

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China.

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OBJECTIVE: The paper aims to evaluate the risk factors for age-related macular degeneration (AMD) in elderly Chinese population in Shenyang, a northeast city of China.

METHODS: A case-control study was conducted to investigate the risk factors for the prevalence of AMD. Ninety three AMD patients diagnosed by a complete ophthalmic examination were recruited as cases from the outpatient departments of two eye hospitals in Shenyang, while 108 normal subjects of similar age and sex were recruited as controls. A questionnaire was administered among both cases and controls.

RESULTS: AMD patients aged 60 years and older accounted for 75.3%. There were significantly higher educational levels, shorter smoking history, less sunlight exposure and cataract, and higher proportion of antioxidants intake in controls than in AMD patients. The frequency of intake of fruits, legumes, fish and shrimps was significantly higher in controls than in AMD patients. In a binary logistic regression analysis, smoking and cataract were the risk factors for AMD (OR: 4.44, 95% CI: 2.27-8.69; OR: 4.47, 95% CI: 2.26-8.85 respectively). The high educational background was a protective factor for AMD (OR: 0.761, 95% CI: 0.51-0.98).

CONCLUSION: A low educational background, smoking and cataract are associated with a higher prevalence of AMD.

PMID: 22108416 [PubMed - in process]

Genetics

Am J Hum Genet. 2011 Nov 16. [Epub ahead of print]

Recessive Mutations in ELOVL4 Cause Ichthyosis, Intellectual Disability, and Spastic Quadriplegia.

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Abstract

Very-long-chain fatty acids (VLCFAs) play important roles in membrane structure and cellular signaling, and their contribution to human health is increasingly recognized. Fatty acid elongases catalyze the first and rate-limiting step in VLCFA synthesis. Heterozygous mutations in ELOVL4, the gene encoding one of the elongases, are known to cause macular degeneration in humans and retinal abnormalities in mice. However, biallelic ELOVL4 mutations have not been observed in humans, and murine models with homozygous mutations die within hours of birth as a result of a defective epidermal water barrier. Here, we report on two human individuals with recessive ELOVL4 mutations revealed by a combination of autozygome analysis and exome sequencing. These individuals exhibit clinical features of ichthyosis, seizures, mental retardation, and spasticity—a constellation that resembles Sjögren-Larsson syndrome (SLS) but presents a more severe neurologic phenotype. Our findings identify recessive mutations in ELOVL4 as the cause of a neuro-ichthyotic disease and emphasize the importance of VLCFA synthesis in brain and cutaneous development.

PMID: 22100072 [PubMed - as supplied by publisher]

PLoS One. 2011;6(11):e27433. Epub 2011 Nov 16.

Characterisation of a C1qtnf5 Ser163Arg Knock-In Mouse Model of Late-Onset Retinal Macular Degeneration.

Shu X, Luhmann UF, Aleman TS, Barker SE, Lennon A, Tulloch B, Chen M, Xu H, Jacobson SG, Ali R, Wright AF.

MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, Edinburgh, United Kingdom.

Abstract

A single founder mutation resulting in a Ser163Arg substitution in the C1QTNF5 gene product causes autosomal dominant late-onset retinal macular degeneration (L-ORMD) in humans, which has clinical and pathological features resembling age-related macular degeneration. We generated and characterised a mouse "knock-in" model carrying the Ser163Arg mutation in the orthologous murine C1qtnf5 gene by site-directed mutagenesis and homologous recombination into mouse embryonic stem cells. Biochemical, immunological, electron microscopic, fundus autofluorescence, electroretinography and laser photocoagulation analyses were used to characterise the mouse model. Heterozygous and homozygous knock-in mice showed no significant abnormality in any of the above measures at time points up to 2 years. This result contrasts with another C1qtnf5 Ser163Arg knock-in mouse which showed most of the features of L-ORMD but differed in genetic background and targeting construct.

PMID: 22110650 [PubMed - in process] PMCID: PMC3217991

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