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MD Research News

Issue 6

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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

Retina. 2010 Nov 30. [Epub ahead of print]

RANIBIZUMAB MONOTHERAPY VERSUS SINGLE-SESSION VERTEPORFIN PHOTODYNAMIC THERAPY COMBINED WITH AS-NEEDED RANIBIZUMAB TREATMENT FOR THE MANAGEMENT OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

Bashshur ZF, Schakal AR, El-Mollayess GM, Arafat S, Jaafar D, Salti HI.

From the *Department of Ophthalmology, American University of Beirut, Beirut, Lebanon; and †Department of Ophthalmology, Hotel Dieu de France, St. Joseph University, Beirut, Lebanon.

Abstract

PURPOSE: To compare verteporfin photodynamic therapy combined with intravitreal ranibizumab (combination therapy) versus ranibizumab monotherapy for management of neovascular age-related macular degeneration.

METHODS: Thirty patients (40 eyes) with neovascular age-related macular degeneration were prospectively allocated to combination therapy or monotherapy. In monotherapy, the induction phase consisted of 3 consecutive monthly ranibizumab injections (0.5 mg), while the combination therapy had a single session of photodynamic therapy with intravitreal ranibizumab. Follow-up treatment for either group consisted only of additional as-needed ranibizumab injections. Main outcome measure was the proportion of eyes losing <15 letters of visual acuity after 12 months.

RESULTS: Except for 1 eye in combination therapy, all eyes in both groups lost <15 letters of visual acuity. At 12 months, there was a mean gain of +12 letters and +3.2 letters for monotherapy and combination therapy, respectively (relative percent change of 32% vs. 7%, P = 0.03). Anatomical improvement was similar in both groups. After induction, the time until ranibizumab re-treatment was longer for combination therapy (P = 0.002) while ranibizumab injections were required more frequently with monotherapy (P = 0.015).

CONCLUSION: Ranibizumab monotherapy showed greater improvement in visual acuity versus combination therapy. However, combination therapy required fewer ranibizumab injections. Larger trials need to confirm the findings of this pilot study.

PMID: 21124254 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging. 2010 Nov 1;41(6):S89-92. doi: 10.3928/15428877-20101031-17.

Fenretinide-associated multilayered retinal hemorrhage in a patient with hairy cell leukemia.

Salehi-Had H, Puliafito CA.

Abstract

Intravenous fenretinide (4-HPR), a cytotoxic retinoid, is being evaluated as part of a phase I clinical trial for patients with hematologic malignancies. In its orally administered form, it is also being evaluated for the treatment of various malignancies and geographic atrophy in subjects with the dry form of age-related macular degeneration. The authors report a case of acute large subretinal and intraretinal hemorrhage noted immediately after initiation of intravenous fenretinide therapy in a patient with hairy cell leukemia. This case highlights the importance of considering multilayered retinal hemorrhage as a possible side effect of fenretinide therapy, especially in patients with underlying hematologic abnormalities.

PMID: 21117610 [PubMed - in process]

Ophthalmic Surg Lasers Imaging. 2010 Nov 1;41(6):S81-4. doi: 10.3928/15428877-20101031-09.

Adult-onset vitelliform detachment unresponsive to monthly intravitreal ranibizumab.

Kandula S, Zweifel S, Freund KB.

Abstract

A 72-year-old woman with decreased visual acuity secondary to an adult-onset vitelliform detachment was treated with three monthly intravitreal injections of 0.5 mg of ranibizumab. Treatment response was monitored by visual acuity and by the eye-tracking feature of the Heidelberg Spectralis spectral domain optical coherence tomography (Heidelberg Engineering, Inc., Carlsbad, CA). There was no improvement in functional or anatomic outcome after three monthly injections of ranibizumab. The eye-tracking feature of the spectral domain optical coherence tomography system was highly accurate in making comparisons between serial optical coherence tomography examinations.

PMID: 21117608 [PubMed - in process]

Genetics

Am J Ophthalmol. 2010 Nov 29. [Epub ahead of print]

ARMS2/HTRA1 Locus Can Confer Differential Susceptibility to the Advanced Subtypes of Age-Related Macular Degeneration.

Sobrin L, Reynolds R, Yu Y, Fagerness J, Leveziel N, Bernstein PS, Souied EH, Daly MJ, Seddon JM.

Department of Ophthalmology, Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts.

Abstract

PURPOSE: To determine if genetic variants that have been associated with age-related macular degeneration (AMD) have a differential effect on the risk of choroidal neovascularization (CNV) and geographic atrophy.

DESIGN: Genetic association study.

METHODS: setting: Multicenter study. study population: Seven hundred forty-nine participants with geographic atrophy and 3209 participants with CNV were derived from 4 AMD studies with similar

procedures from Tufts Medical Center, the Age-Related Eye Disease Study, University of Utah, and Hopital Intercommunal de Creteil. procedures: AMD grade was assigned based on fundus photography and examination using the clinical age-related maculopathy staging system. All samples were genotyped for single nucleotide polymorphisms (SNPs) previously associated with AMD. Allele frequencies were compared between participants with CNV and geographic atrophy using PLINK within each cohort and Mantel-Haenszel meta-analysis was performed to combine odds ratios (OR). main outcome measures: Differences in allele frequencies between participants with geographic atrophy and CNV.

RESULTS: The frequency of the T allele of ARMS2/HTRA1 rs10490924 was significantly higher in participants with CNV than in those with geographic atrophy (OR, 1.37; 95% confidence interval, 1.21-1.54; P value = 4.2 × 10(-7)). This result remained statistically significant when excluding individuals who had geographic atrophy in 1 eye and CNV in the contralateral eye (P = 2.2 × 10(-4)). None of the other SNPs showed a significant differential effect for CNV vs geographic atrophy, including CFH, C2/CFB, C3, CFI, LIPC, and TIMP3.

CONCLUSIONS: Genetic variation at the ARMS2/HTRA1 locus confers a differential risk for CNV vs geographic atrophy in a well-powered sample.

PMID: 21122828 [PubMed - as supplied by publisher]

Neurosci Lett. 2010 Nov 23. [Epub ahead of print]

Correlation of Complement Factor H Gene Polymorphisms with Exudative Age-related Macular Degeneration in a Chinese Cohort.

Dong L, Qu Y, Jiang H, Dai H, Zhou F, Xu X, Bi H, Pan X, Dang G.

Clinical Medical Department of Medical School, Shandong University, Jinan, China, Department of Ophthalmology.

Abstract

AIMS: To evaluate the association between Complement Factor H (CFH) gene polymorphism and the risk of exudative age-related macular degeneration (AMD) in a case-control study in a Chinese cohort. 136 exudative AMD patients and 140 age- and sex-matched control subjects were recruited.

METHODS: We genotyped 3 common single nucleotide polymorphisms (SNPs), namely, -257C>T (rs3753394), Y402H (rs1061170) and IVS15 (rs1329428), genetic analyses were performed on all available genotype data. All the possible haplotypes of these 3 SNPs were detected. Polymerase chain reaction (PCR) and allele-specific restriction endonuclease digestion were performed, some PCR products of these 3 SNPs were sequenced.

RESULTS: The risk alleles (T, C or G) of the 3 SNPs conferred 1.72 fold, 3.14 fold, and 1.79 fold of increased likelihood of the disease respectively (P<0.05). The heterozygous genotype in rs1061170 (TC) revealed significant association, meanwhile rs3753394 and rs1329428 had a slight association with the disease respectively. Significant differences were shown in the risk alleles in the 3 SNPs among different Chinese cohort. Low linkage disequilibrium was found among the 3 SNPs. The haplotypes TCG and CTG revealed as risk factors, whereas the protective haplotype CTA was over-represented in controls.

CONCLUSIONS: We found significantassociation between risk alleles (T, C or G) of the 3 SNPs and the disease. The genetic divergence across multiple populations within Chinese existed. Risk haplotypes and protective haplotype were found in this study.

PMID: 21111031 [PubMed - as supplied by publisher]

Other treatment

Klin Oczna. 2010;112(7-9):230-5.

[Autologous choroidal RPE patch transplantation for submacular hemorrhage in age-related macular degeneration].

[Article in Polish]

Stopa M, Rospond-Kubiak I, Rakowicz P, Kociecki J.

Z Katedry i Kliniki Okulistyki Uniwersytetu Medycznego w Poznaniu. stopa@usoms.poznan.pl

Abstract

PURPOSE: To report autologous choroidal RPE patch transplantation for treatment of submacular hemorrhage in a patients with age related macular degeneration.

MATERIAL AND METHODS: A case report of a patient with sudden vision deterioration due to submacular hemorrhage in AMD. The visual acuity was 5/5 in the right eye and 0.5/50 in the left eye. He was treated with autologous choroidal RPE patch transplantation. Outcome measures included preoperative and postoperative visual acuity at 1, 3, 6 months, duration of hemorrhage, hemorrhage size on preoperative fluorescein angiography and thickness of the subretinal hemorrhagic complex on preoperative and postoperative OCT scans.

RESULTS: Visual acuity improved from 0.5/50 to 5/50 in 6 months follow-up. No major intraoperative and postoperative complications were observed. The perfusion of the graft was confirmed in ICG angiography.

CONCLUSIONS: Autologous choroidal RPE patch transplantation is an effective option for submacular hemorrhage treatment in AMD. Unlike macular translocation, the surgery can be performed even in patients with excellent visual acuity in the fellow eye.

PMID: 21121126 [PubMed - in process]

Mol Ther. 2010 Nov 30. [Epub ahead of print]

Preclinical Safety Evaluation of AAV2-sFLT01- A Gene Therapy for Age-related Macular Degeneration.

Maclachlan TK, Lukason M, Collins M, Munger R, Isenberger E, Rogers C, Malatos S, Dufresne E, Morris J, Calcedo R, Veres G, Scaria A, Andrews L, Wadsworth S.

Genzyme Corporation, Framingham, Massachusetts, USA.

Abstract

AAV2-sFLT01 is a vector that expresses a modified soluble Flt1 receptor designed to neutralize the proangiogenic activities of vascular endothelial growth factor (VEGF) for treatment of age-related macular degeneration (AMD) via an intravitreal injection. Owing to minimal data available for the intravitreal route of administration for adeno-associated virus (AAV), we initiated a 12-month safety study of AAV2-sFLT01 administered intravitreally at doses of 2.4 × 10(9) vector genomes (vg) and 2.4 × 10(10) vg to cynomolgus monkeys. Expression of sFlt01 protein peaked at ~1-month postadministration and remained relatively constant for the remainder of the study. Electroretinograms, fluorescein angiograms, and tonometry were assessed every 3 months, with no test article-related findings observed in any group. Indirect ophthalmoscopy and slit lamp exams performed monthly revealed a mild to moderate but self-resolving vitreal inflammation in the high-dose group only, which follow-up studies suggest was directed against the AAV2 capsid. Histological evaluation revealed no structural changes in any part of the eye and occasional inflammatory cells in the trabecular meshwork, vitreous and retina in the high-dose group. Biodistribution analysis in rats and monkeys found only trace amounts of vector outside the injected eye. In summary,

these studies found AAV2-sFLT01 to be well-tolerated, localized, and capable of long-term expression.

PMID: 21119620 [PubMed - as supplied by publisher]

Ther Apher Dial. 2010 Dec;14(6):608-9. doi: 10.1111/j.1744-9987.2010.00892.x.

Reply to letter to the editor: best-available evidence supports the use of rheopheresis for high-risk dry age-related macular degeneration.

Klingel R, Koch FH, Kirchhof B.

Apheresis Research Institute, Cologne, Department of Ophthalmology, University of Frankfurt, and Department of Vitreo-Retinal Surgery, University of Cologne, Germany E-mail: afi@apheresis-research.de.

PMID: 21118373 [PubMed - in process]

Ther Apher Dial. 2010 Dec;14(6):607-8. doi: 10.1111/j.1744-9987.2010.00879.x. Epub 2010 Oct 29.

No evidence to support the use of plasmapheresis for age-related macular degeneration.

Finger RP, Krohne TU, Charbel Issa P, Scholl HP, Holz FG.

Department of Ophthalmology, University of Bonn, Bonn, Germany Wilmer Eye Institute, Johns Hopkins University, Maryland, USA; Nuffield Laboratory, Department of Ophthalmology, Oxford University, Oxford, UK Email: robert.finger@ukb.uni-bonn.de.

PMID: 21118372 [PubMed - in process]

Ophthalmic Surg Lasers Imaging. 2010 Nov 1;41(6):S85-8. doi: 10.3928/15428877-20101031-10.

Acute Severe Visual Decrease After Photodynamic Therapy with Verteporfin: Spectral-Domain OCT Features.

Keane PA, Aghaian E, Ouyang Y, Chong LP, Sadda SR.

Abstract

In this report, spectral-domain optical coherence tomography (OCT) was used to characterize the acute morphologic alterations that occur when photodynamic therapy with verteporfin results in an acute severe visual decrease. The clinical and imaging records of a patient with neovascular age-related macular degeneration who suffered this complication were reviewed. Using spectral-domain OCT, two relatively distinct subretinal fluid compartments were visualized: a sparsely hyperreflective pocket of subretinal fluid overlying the fibrovascular pigment epithelial detachment, consistent with fibrinous exudation, and a more homogenously hyporeflective compartment at the periphery of the choroidal neovascular lesion, consistent with serous exudation. The higher axial resolution, and greater sensitivity, of spectral-domain OCT allows improved visualization of the subretinal space. As experience with spectral-domain OCT grows, new parameters will emerge-such as those related to subretinal fluid-that will facilitate improvements in both the qualitative and quantitative evaluation of macular disease.

PMID: 21117609 [PubMed - in process]

Ophthalmic Surg Lasers Imaging. 2010 Nov 1;41(6):S6-S14. doi: 10.3928/15428877-20101031-19.

Spectral domain optical coherence tomography imaging of dry age-related macular degeneration.

Yehoshua Z, Rosenfeld PJ, Gregori G, Penha F.

Abstract

Spectral domain optical coherence tomography is a useful new technology for imaging and measuring geographic atrophy (GA) and drusen, the hallmarks of dry age-related macular degeneration (AMD). The advantage of using this novel technique over other imaging modalities for dry AMD is that the same scan pattern can be used to image both drusen and GA while obtaining reproducible, quantitative data on both the area of GA and the morphologic features of drusen. Moreover, this strategy enables the clinician to follow the disease as it progresses from drusen to both GA and choroidal neovascularization. No other imaging modality is able to quantitatively assess all forms of AMD. This unique feature of spectral domain optical coherence tomography makes it the ideal imaging modality for clinical trials designed to assess new drugs for the treatment of dry AMD.

PMID: 21117603 [PubMed - in process]

Ophthalmic Surg Lasers Imaging. 2010 Nov 1;41(6):S28-33. doi: 10.3928/15428877-20101031-14.

Measurement of subfoveal choroidal thickness using spectral domain optical coherence tomography.

McCourt EA, Cadena BC, Barnett CJ, Ciardella AP, Mandava N, Kahook MY.

Abstract

BACKGROUND AND OBJECTIVE: To compare subfoveal choroidal thickness (SFCT) in normal patients and those with known ocular pathology using spectral domain optical coherence tomography (SD-OCT).

PATIENTS AND METHODS: This retrospective, observational case series was conducted at a tertiary care center where 194 consecutive eyes from 102 patients were imaged. Patients were not included or excluded based on presence or absence of pathology. One masked observer imaged the choroid and a second masked observer measured SFCT. Multivariate analysis was used and a statistical model created to analyze the changes in SFCT induced by age, diabetic retinopathy, glaucoma, wet and dry age-related macular degeneration, and other posterior pole pathology.

RESULTS: The mean SFCT of the 194 eyes studied was 246.59 ± 93.17 μm with a mean age of 55.50 ± 19.70 years. A strong negative relationship was found between age and SFCT (R(2) = 0.42), with an average 3.09-μm decrease in SFCT per additional year of age. Subgroup analysis demonstrated that patients with diabetic retinopathy, wet or dry age-related macular degeneration, and glaucoma all had SFCT measurements that were statistically significantly less than those of normal patients. However, when regression analysis was used to control for age, this difference was no longer significant.

CONCLUSION: No differences were found in SFCT in patients with glaucoma, macular degeneration, or diabetic retinopathy compared to eyes lacking pathology when age was counted as a confounding variable. Age has a strong inverse relationship with SFCT, independently confirming prior studies and creating a foundation for more research on the relationship between ocular pathology and choroidal thickness.

PMID: 21117598 [PubMed - in process]

Ophthalmic Surg Lasers Imaging. 2010 Nov 1;41(6):S104-8. doi: 10.3928/15428877-20101031-07.

Assessing the Photoreceptor Mosaic over Drusen Using Adaptive Optics and SD-OCT.

Godara P, Siebe C, Rha J, Michaelides M, Carroll J.

Abstract

Drusen are extracellular deposits that accumulate between the retinal pigment epithelium and Bruch's membrane. They are one of the earliest clinical manifestations of age-related macular degeneration and it is thought that they disrupt the overlying photoreceptors, leading to subsequent vision loss. The purpose of

this study was to illustrate how spectral domain optical coherence tomography and adaptive optics fundus imaging can be used to quantitatively analyze the integrity of the overlying photoreceptors in a single subject with macular drusen. This imaging approach and the image analysis metrics introduced may serve as the foundation for valuable imaging-based biomarkers for detecting the earliest stages of disease, tracking progression, and monitoring treatment response.

PMID: 21117594 [PubMed - in process]

Klin Oczna. 2010;112(7-9):223-9.

Combined therapy in exudative age-related macular degeneration.

Figurska M, Wierzbowska J, Robaszkiewicz J.

Department of Ophthalmology, Military Health Service Institute, Warsaw. malgorzata-figurska@wp.pl

Abstract

PURPOSE: Therapeutic options in active exudative age-related macular degeneration (AMD) are following means used to destroy the choroidal neovascularization (CNV) lesion: laser photocoagulation, radiotherapy, transpupillary thermotherapy, photodynamic therapy (POT) or removal of neovascular membrane through vitreoretinal surgery. Another possibility is to suppress the development of neovasculanization through intravitreal administration of anti-VEGF agents: ranibizumab, bevacizumab (off-label), sodium pegaptanib or steroids (off-label). The aim of this paper is to present the early phase of treating exudative AMO with combined therapy: photodynamic therapy with intravitreal ranibizumab injection.

MATERIAL AND METHODS: Our observation is based on three clinical cases. Observations are being carried out on larger patient groups according to the treatment scheme presented in this paper.

RESULTS: In the three cases described one POT procedure and the saturation phase of three ranibizumab injections allowed a significant improvement in visual acuity and closure of CNV leakage confirmed by fluorescein angiography (FA) and optical coherence tomography (OCT). Treatment is being continued according to AMO activity: next POT in case of leakage in FA, another ranibizumab injection according to PRONTO study reinjection criteria.

CONCLUSIONS: The pathomechanism of exudative AMB confirms reasonability of combined treatment. Considering the stages of neovascularization in exudative AMO. VEGF inhibition combined with POT has a synergistic action and increases the effectiveness of both therapies alone. L.arge clinical studies (FOCUS) show that combined therapy reduces the number or required POT procedures. In combined therapy modification of POT parameters should be considered: reduction of energy and laser exposure time.

PMID: 21117365 [PubMed - in process]

Klin Oczna. 2010;112(7-9):210-2.

Age related macular degeneration and presence of posterior vitreous detachment.

Gawecki M, Doroszkiewicz M, Rydzewski J.

Department of Ophthalmology, Specialist Hospital, Chojnice. gawecki@use.pl

Abstract

PURPOSE: To find correlation between presence of PVD and incidence of different forms of AMD.

MATERIAL AND METHODS: 210 eyes of patients with AMD were examined. Fluorescein angiography determined type of AMD and ultrasound examination evaluated presence of PVD. Control group included

164 eyes of patients routinely admitted to the hospital for cataract surgery. Inclusion criterium was lack of AMD and retinal medical history.

RESULTS: In the control group prevalence of PVD was higher in women than in men--respectively 50.5% and 23.6%. PVD was more frequent in male patients with dry AMD (50%) than in male controls (23.6%). PVD was also more frequent in female patients with dry form of AMD (69.2%) than in controls (50.5%). In female group with AMD PVD was more frequent in patients with dry form of AMD than in patients with wet form of AMD (69.2% and 44.8%). In patients with dry AMD, PVD was statistically more frequent in women (69.2%) than in men (50%). Statistically significant was the difference between prevalence of PVD in dry and wet group (male and females together)--60.7% in dry AM and 42.6% ind wet AMD.

CONCLUSION: Persistence of vitreal adhesion and traction with age might lead to a shift of the dry form into wet form of AMD. Detachment of the vitreous in dry AMD might secure the persistence of dry form. Women, due to early PVD are more prone to complications resulting from vitreoretinal traction.

PMID: 21117364 [PubMed - in process]

Bull Soc Belge Ophtalmol. 2010;(315):31-8.

An evaluation of the young people's knowledge regarding the ophthalmic effects of smoking.

Kanonidou E, Konidaris V, Kanonidou C, Praidou A.

Department of Ophthalmology, General Hospital of Veria, Veria, Greece. evkanon@hotmail.com

Abstract

PURPOSE: To assess the young people's knowledge regarding the ophthalmic effects of smoking.

METHODS: 198 students (111 males and 87 females) with a mean age of 27 years old (+/- 6 years) participated in the study. A simple questionnaire was used and the participants were requested to fill out the questionnaire themselves.

RESULTS: 77% (152) of the participants were smokers. 67% (130) have never heard about the adverse effect of smoking to the eyes. 87% (172) have not heard about the relationship between smoking and thyroid eye disease. 84% (166) were not aware that smoking could ccontribute to the formation of cataract. 50% (99) have no knowledge about the association between smoking and age-related macular degeneration. 80% (158) were unaware that smoking is a risk factor for visual loss.

CONCLUSIONS: The level of knowledge of young people regarding the ophthalmic effects of smoking is not satisfactory. There is an urgent need to promote the awareness of the population regarding the adverse effect of smoking on visual function.

PMID: 21110508 [PubMed - in process]

Pathogenesis & epidemiology

Graefes Arch Clin Exp Ophthalmol. 2010 Dec 3. [Epub ahead of print]

The significance of the complement system for the pathogenesis of age-related macular degeneration - current evidence and translation into clinical application.

Charbel Issa P, Victor Chong N, Scholl HP.

Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, UK.

Abstract

BACKGROUND: Dysregulation of the complement system has been shown to play a major role in the pathogenesis of age-related macular degeneration (AMD).

METHODS: The current evidence from human studies derives from immunohistochemical and proteomic studies in donor eyes, genetic association studies, and studies of blood complement protein levels. These lines of evidence are corroborated by in vitro and animal studies.

RESULTS: In AMD donor eyes, detection of complement proteins in drusen suggested local inflammatory processes involving the complement system. Moreover, higher levels of complement proteins in the Bruch's membrane/choroid complex could be detected in AMD donor eyes compared to controls. A large number of independent genetic studies have consistently confirmed the association of AMD with risk or protective variants in genes coding for complement proteins, including complement factor H (CFH), CFH-related proteins 1 and 3, factor B/C2, C3 and factor I. Another set of independent studies detected increased levels of complement activation products in plasma of AMD patients, suggesting that AMD may be a systemic disease and the macula a vulnerable anatomic site of minimal resistance to complement activation. Genotype-phenotype correlations, including the impact of genetic variants on disease progression, gene-environment and pharmacogenetic interactions, have been investigated. There is evidence that complement gene variants may be associated with the progression from early to late forms of AMD, whereas they do not appear to play a significant role when late atrophic AMD has already developed. There are indications for an interaction between genetic variants and supplementation and dietary factors. Also, there is some evidence that variants in the CFH gene influence treatment effects in patients with neovascular AMD.

CONCLUSIONS: Such data suggest that the complement system may have a significant role for developing new prophylactic and therapeutic interventions in AMD. In fact, several compounds acting on the complement pathway are currently in clinical trials. Therapeutics that modulate the complement system need to balance inhibition with preservation of sufficient functional activity in order to maintain adequate immune responses and tissue homeostasis. Specifically, targeting the dysfunction appears more adequate than a global suppression of complement activation in chronic diseases such as AMD.

PMID: 21127893 [PubMed - as supplied by publisher]

Ophthalmology. 2010 Nov 30. [Epub ahead of print]

Prevalence of Age-related Macular Degeneration in Old Persons: Age, Gene/Environment Susceptibility Reykjavik Study.

Jonasson F, Arnarsson A, Eiríksdottir G, Harris TB, Launer LJ, Meuer SM, Klein BE, Klein R, Gudnason V, Cotch MF.

Ophthalmology, Landspitali University Hospital, Iceland; Faculty of Medicine, University of Iceland, Reykjavik, Iceland.

Abstract

PURPOSE: To describe the prevalence and signs of early and late age-related macular degeneration (AMD) in an old cohort.

DESIGN: Population-based cohort study.

PARTICIPANTS: We included 5272 persons aged ≥66 years, randomly sampled from the Reykjavik area.

METHODS: Fundus images were taken through dilated pupils using a 45-degree digital camera and graded for drusen size, type, area, increased retinal pigment, retinal pigment epithelial depigmentation, neovascular lesions, and geographic atrophy (GA) using the modified Wisconsin Age-Related Maculopathy Grading System.

MAIN OUTCOME MEASURES: Age-related macular degeneration in an elderly cohort.

RESULTS: The mean age of participants was 76 years. The prevalence of early AMD was 12.4% (95% confidence interval [CI], 11.0-13.9) for those aged 66 to 74 years and 36% (95% CI, 30.9-41.1) for those aged ≥85 years. The prevalence of exudative AMD was 3.3% (95% CI, 2.8-3.8). The prevalence of pure GA was 2.4% (95% CI, 2.0-2.8). The highest prevalence of late AMD was among those aged ≥85 years: 11.4% (95% CI, 8.2-14.5) for exudative AMD and 7.6% (95% CI, 4.8-10.4) for pure GA.

CONCLUSIONS: Persons aged ≥85 years have a 10-fold higher prevalence of late AMD than those aged 70 to 74 years. The high prevalence of late AMD in the oldest age group and expected increase of elderly people in the western world in coming years call for improved preventive measures and novel treatments.

FINANCIAL DISCLOSURE(S): The author(s) have no proprietary or commercial interest in any materials discussed in this article.

PMID: 21126770 [PubMed - as supplied by publisher]

J Neuroinflammation. 2010 Dec 2;7(1):87. [Epub ahead of print]

CCL2/CCR2 and CX3CL1/CX3CR1 chemokine axes and their possible involvement in age-related macular degeneration.

Raoul W, Auvynet C, Camelo S, Guillonneau X, Feumi C, Combadiere C, Sennlaub F.

Abstract

ABSTRACT: The causes of age-related macular degeneration (AMD) are not well understood. Due to demographic shifts in the industrialized world a growing number of people will develop AMD in the coming decades. To develop treatments it is essential to characterize the disease's pathogenic process. Over the past few years, numerous studies have focused on the role of chemotactic cytokines, also known as chemokines. Certain chemokines, such as CCL2 and CX3CL1, appear to be crucial in subretinal microglia and macrophage accumulation observed in AMD, and participate in the development of retinal degeneration as well as in choroidal neovascularization. This paper reviews the possible implications of CCL2 and CX3CL1 signaling in AMD. Expression patterns, single nucleotide polymorphisms (SNPs) association studies, chemokine and chemokine receptor knockout models are discussed. Future AMD treatments could target chemokines and/or their receptors.

PMID: 21126357 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2010 Dec;51(12):6868-74.

Scene perception in age-related macular degeneration.

Tran TH, Rambaud C, Despretz P, Boucart M.

Laboratoire de Neurosciences et Pathologies Fonctionnelles, CNRS, Université Lille Nord de France, Lille, France.

Abstract

Purpose. To assess the scene gist recognition in eyes with age-related macular degeneration (AMD) and to study the relationship between scene recognition and macular function. Methods. Twenty-seven patients with age-related macular degeneration with a visual acuity lower than 20/50 and 17 age-matched controls were included. All patients underwent a visual field test, fundus autofluorescence, and fluorescein angiography to assess the visual field defect and the lesion size. The stimuli were colored photographs of natural scenes displayed on a 30-inch screen. Two scene categorization tasks were performed: natural versus urban and indoor versus outdoor scenes. Participants were given a target (e.g., indoor scenes) and asked to press a key when they saw a picture corresponding to that target. Accuracy and response times were recorded. Results. Patients with AMD were able to accomplish both categorization tasks with a high

correct detection rate (above 75% correct), though performance was lower than in controls for both natural/urban scenes and indoor/outdoor scenes. Patients with AMD were more accurate and faster for natural/urban scenes than for indoor/outdoor scenes, but performance did not differ between the two categories in controls. No significant correlation was found between performance for scene categorization and clinical variables such as visual acuity, type of AMD, size of the scotoma, and size of the lesion. Conclusions. Scene gist recognition can be accomplished with the low spatial resolution of peripheral vision. These results support the "scene-centered approach" that initial scene recognition is based on the global scene properties and not on the objects it contains.

PMID: 21123770 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2010 Dec;51(12):6715-21.

Performance of drusen detection by spectral-domain optical coherence tomography.

Schlanitz FG, Ahlers C, Sacu S, Schütze C, Rodriguez M, Schriefl S, Golbaz I, Spalek T, Stock G, Schmidt-Erfurth U.

Department of Ophthalmology, Medical University of Vienna, Vienna, Austria.

Abstract

Purpose. To evaluate the performance of automated analyses integrated in three spectral-domain optical coherence tomography (SD-OCT) devices to identify drusen in eyes with early (i.e., nonatrophic and nonneovascular) age-related macular degeneration (AMD). Methods. Twelve eyes of 12 AMD patients, classified as AREDS 2 and 3 and having a mean count of 113 drusen were examined with three clinical SD-OCT devices (Cirrus [Carl Zeiss Meditec, Dublin CA], 3DOCT-1000 [Topcon, Tokyo, Japan], and Spectralis [Heidelberg Engineering, GmbH, Heidelberg, Germany]) and five different scan patterns. After standard automated segmentation of the RPE was performed, every druse in each B-scan was identified and graded by two independent expert graders. Errors in the segmentation performance were classified as negligible, moderate, or severe. Correlations were based on the diameter and height of the druse and its automated segmentation. The overall drusen pattern identified by experts' detailed delineation was plotted with a custom-made computer program to compare automated to manual identification outcomes. Results. A total of 1356 drusen were analyzed. The automated segmentation of the retinal pigment epithelium (RPE) by Cirrus made significantly fewer errors in detecting drusen than did the 3DOCT-1000 ($P < 0.001$). The Cirrus 200 × 200 scan pattern detected 30% of the drusen with negligible errors. Spectralis did not offer a true RPE segmentation. The drusen counts by expert graders were significantly higher in the scans than in the standard fundus photographs ($P < 0.05$). Conclusions. SD-OCT imaging proved an excellent performance in visualizing drusen-related RPE disease. However, the available automated segmentation algorithms showed distinct limitations to reliable identification of the amount of drusen, particularly smaller drusen, and the actual size.

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New focus on alpha-crystallins in retinal neurodegenerative diseases.

Fort PE, Lampi KJ.

Department of Ophthalmology, Penn State University, Integrative Biosciences, Oregon Health & Science University, Hershey, PA 17033, United States.

Abstract

The crystallin proteins were initially identified as structural proteins of the ocular lens and have been recently demonstrated to be expressed in normal retina. They are dramatically upregulated by a large

range of retinal diseases including diabetic retinopathy, age-related macular degeneration, uveitis, trauma and ischemia. The crystallin family of proteins is composed of alpha-, beta- and gamma-crystallin. Alpha-crystallins, which are small heat shock proteins, have received substantial attention recently. This review summarizes the current knowledge of alpha-crystallins in retinal diseases, their roles in retinal neuron cell survival and retinal inflammation, and the regulation of their expression and activity. Their potential role in the development of new treatments for neurodegenerative diseases is also discussed.

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Calcium Overload Is A Critical Step in Programmed Necrosis of ARPE-19 Cells Induced by High-Concentration H(2)O(2).

Li GY, Fan B, Zheng YC.

Department of Ophthalmology, Second Hospital of Jilin University, Changchun 130041, Jilin, China.

Abstract

OBJECTIVE: Oxidative stress plays an important role in retinal pigmental epithelium (RPE) death during aging and the development of age-related macular degeneration. Although early reports indicate that reactive oxygen species (ROS) including H(2)O(2) can trigger apoptosis at lower concentrations and necrosis at higher concentrations, the exact molecular mechanism of RPE death is still unclear. The purpose of this study was to investigate the molecular pathways involved in RPE death induced by exogenous ROS, especially at higher concentrations.

METHODS: Cultured ARPE-19 cells were treated with H(2)O(2) at different concentrations and cell viability was measured with the MTT assay. Cell death was morphologically studied by microscopy using APOPercentage assay and PI staining. Furthermore, the impact of oxidative stress on ARPE-19 cells was assessed by HO-1 and PARP-1 Western blotting and by the protection of antioxidant EGCG. Calcium influx was determined using the fura-2 calcium indicator and the role of intracellular calcium overload in ARPE-19 cell death was evaluated following cobalt treatment to block calcium effects.

RESULTS: H(2)O(2) reduced the viability of ARPE-19 cells in a concentration-dependent manner, which was presented as a typical s-shaped curve. Cell death caused by high concentrations of H(2)O(2) was confirmed to be programmed necrosis. Morphologically, dying ARPE-19 cells were extremely swollen and lost the integrity of their plasma membrane, positively detected with APOPercentage assay and PI staining. 24-hour treatment with 500 μmol/L H(2)O(2) induced remarkable up-regulation of HO-1 and PARP-1 in ARPE-19 cells. Moreover, antioxidant treatment using EGCG effectively protected cells from H(2)O(2)-induced injury, increasing cell viability from 14.17%±2.31% to 85.77%±4.58%. After H(2)O(2) treatment, intracellular calcium levels were highly elevated with a maximum concentration of 1200nM. Significantly, the calcium channel inhibitor cobalt was able to blunt this calcium influx and blocked the necrotic pathway, rescuing the ARPE-19 cell from H(2)O(2)-induced death.

CONCLUSIONS: At high concentrations, H(2)O(2) induces ARPE-19 cell death through a regulated necrotic pathway with calcium overload as a critical step in the cell death program.

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