

Issue 37

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Drug treatment

Ophthalmologica. 2011 Jul 13. [Epub ahead of print]

One-Year Results of Intravitreal Ranibizumab with or without Photodynamic Therapy for Polypoidal Choroidal Vasculopathy.

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Purpose: To evaluate the safety and efficacy of intravitreal ranibizumab with or without photodynamic therapy (PDT) in the treatment of polypoidal choroidal vasculopathy (PCV) in Korean patients.

Methods: A retrospective chart review of 22 patients (24 eyes) with PCV was conducted. Nine eyes were treated with intravitreal ranibizumab combined with a single session of PDT (group 1), and 15 eyes were treated only with ranibizumab (group 2). Such clinical evaluations as best-corrected Snellen visual acuity, central retinal thickness (CRT) by optical coherence tomography (OCT), fluorescein angiography (FA) and indocyanine green angiography (ICGA) were done at baseline, 1, 3, 6, 9 and 12 months after the first injections. Ranibizumab was reinjected on an as-needed basis guided by OCT, FA and ICGA, or at the doctor's discretion.

Results: The mean follow-up duration was 22.5 months (range 12-37). The mean best-corrected visual acuity (logMAR) improved, and the mean CRT decreased throughout 12 months in both groups; no statistically significant difference between the groups was found ($p = 0.327$, $p = 0.073$, respectively). The number of ranibizumab injections was not significantly different either ($p = 0.555$).

Conclusions: Intravitreal ranibizumab with or without PDT for PCV in Korean patients resulted in visual and anatomical improvement over the 1-year follow-up period.

PMID: 21757883 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2011;5:771-81. Epub 2011 Jun 9.

Retinal vein occlusion and macular edema - critical evaluation of the clinical value of ranibizumab.

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Abstract

Retinal vein occlusions (RVOs) constitute the second most common cause of retinal vascular disease after diabetic retinopathy, with a prevalence of between 1% and 2% in persons older than 40 years of age. Despite the existence of numerous potential therapeutic options, none is entirely satisfactory, and many patients with RVO suffer irreversible visual loss. Fortunately however, the recent introduction of antivascular endothelial growth factor (VEGF) agents, such as ranibizumab (Lucentis®), Genentech, South San Francisco, CA) and bevacizumab (Avastin®), Genentech), offers a potentially new treatment approach for clinicians managing this disorder. The results of the BRAVO and CRUISE trials have provided the first definitive evidence for the efficacy and safety of ranibizumab in the treatment of RVO. As a result, ranibizumab has recently been approved by the US Food and Drug Administration for the treatment of RVO-associated macular edema. In this review, we provide a critical evaluation of clinical trial data for the safety and efficacy of ranibizumab, and address unresolved issues in the management of this disorder.

PMID: 21750610 [PubMed]

Am J Ophthalmol. 2011 Jul 8. [Epub ahead of print]

A Randomized Pilot Study of Low-Fluence Photodynamic Therapy Versus Intravitreal Ranibizumab for Chronic Central Serous Chorioretinopathy.

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PURPOSE: To report 6-month outcomes of a prospective, randomized study comparing the efficacy and safety between low-fluence photodynamic therapy (PDT) and intravitreal injections of ranibizumab in the treatment of chronic central serous chorioretinopathy.

DESIGN: Prospective, randomized, single-center pilot study.

METHODS: Sixteen eyes with chronic central serous chorioretinopathy were randomized to receive either low-fluence PDT or intravitreal injections of ranibizumab: 8 eyes in the low-fluence PDT group and 8 in the ranibizumab group. Rescue treatment was considered if subretinal fluid was sustained after completion of primary treatment: low-fluence PDT for the ranibizumab group and ranibizumab injection for the low-fluence PDT group. Main outcome measures were excess foveal thickness, resolution of subretinal fluid, choroidal perfusion on indocyanine green angiography, and best-corrected visual acuity.

RESULTS: At 3 months, the mean excess foveal thickness was reduced from $74.1 \pm 56.0 \mu\text{m}$ to $-35.4 \pm 44.5 \mu\text{m}$ in the low-fluence PDT group ($P = .017$) and from $26.3 \pm 50.6 \mu\text{m}$ to $-23.1 \pm 56.5 \mu\text{m}$ in the ranibizumab group ($P = .058$). After a single session of PDT, 6 eyes (75%) in the low-fluence PDT group achieved complete resolution of subretinal fluid and reduction of choroidal hyperpermeability, whereas 2 (25%) eyes in the ranibizumab group achieved this after consecutive ranibizumab injections. Four eyes (50%) in the ranibizumab group underwent additional low-fluence PDT and accomplished complete resolution. At 3 months, significant improvement of best-corrected visual acuity was not demonstrated in the low-fluence PDT group ($P = .075$), whereas it was observed in the ranibizumab group ($P = .012$). However, the tendency toward improvement of best-corrected visual acuity was not maintained.

CONCLUSIONS: In terms of anatomic outcomes, the effect of ranibizumab injections was not promising compared with that of low-fluence PDT.

PMID: 21742303 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Invest Ophthalmol Vis Sci. 2011 Jul 14. [Epub ahead of print]

Progression of age-related geographic atrophy: Role of the fellow-eye.

Fleckenstein M, Schmitz-Valckenberg S, Adrion C, Visvalingam S, Göbel AP, Mössner A, von Strachwitz CN, Mackensen F, Pauleikhoff D, Wolf S, Mansmann U, Holz FG; for the FAM Study Group.

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Purpose: To evaluate the role of the fellow-eye status for progression of geographic atrophy (GA) in patients with age-related macular degeneration (AMD).

Methods: A total of 300 eyes with GA of 193 patients from the prospective, longitudinal natural history FAM-Study (NCT00393692) were classified into 3 groups according to the AMD manifestation of the fellow-eye at baseline examination: (1) bilateral GA, (2) early/intermediate AMD, and (3) exudative AMD. GA areas were quantified based on fundus autofluorescence images using a semi-automated image processing method and progression rates (PR) were estimated using 2-level linear mixed effects-models.

Results: Crude GA-PR in the bilateral GA group (mean 1.64mm(2)/year, 95%CI[1.478;1.803]) was significantly higher compared to the fellow-eye early/intermediate group (0.74mm(2)/year [0.146;1.342]). Although there was significant difference in baseline GA-size ($p=0.0013$, t-test), and there was a significant increase of GA-PR by 0.11mm(2)/year (95%CI[0.05;0.17]) per one disc area (1DA=2.54mm(2)), an additional mean change of -0.79 (95%CI[-1.43;-0.15]) was given to the PR beside the effect of baseline GA-size. However, this difference was only significant when GA-size was ≥ 1 DA at baseline with a GA-PR of 1.70mm(2)/year, 95%CI[1.54;1.85] in the bilateral and 0.95mm(2)/year [0.37;1.54] in the early/intermediate group. There was no significant difference in PR comparing with the fellow-eye exudative group.

Conclusions: The results indicate that the AMD manifestation of the fellow-eye at baseline serves as an indicator for disease progression in eyes with $GA \geq 1$ DA. Predictive characteristics may not only contribute to the understanding of pathophysiological mechanisms, but are also useful for the design of future interventional trials in GA patients.

PMID: 21757586 [PubMed - as supplied by publisher]

Ophthalmic Res. 2011 Jul 13;47(2):81-86. [Epub ahead of print]

Drusen Characteristics Revealed by Spectral-Domain Optical Coherence Tomography and Their Corresponding Fundus Autofluorescence Appearance in Dry Age-Related Macular Degeneration.

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Purpose: To analyze the relationship between drusen morphology revealed by spectral-domain optical coherence tomography (SD-OCT) and corresponding fundus autofluorescence (FAF) features of the same drusen using the Heidelberg Retina Angiograph 2 (HRA2), in patients with dry age-related macular degeneration (AMD).

Methods: Dry AMD patients were imaged with SD-OCT and HRA2 on the same day. SD-OCT B scans were then precisely overlaid onto the HRA2 images, and the SD-OCT morphological characteristics of the drusen were correlated with the corresponding FAF appearance. The analyzed morphological features of the drusen included: size, status of the inner segment/outer segment (IS-OS) junctional layer above the drusen, shape of the drusen, internal reflectivity, homogeneity and presence of overlaying hyperreflective foci. The FAF characteristics of each druse were rated as hyperautofluorescent, hypoautofluorescent or

normally autofluorescent. Spearman's correlation coefficient was used to analyze the correlation between the 2 primary outcomes: SD-OCT morphology of the drusen and their autofluorescent appearance.

Results: 431 drusen in 32 eyes of 16 dry AMD patients were evaluated. Of the 7 morphological characteristics assessed by SD-OCT, only drusen size and the status of the IS-OS layer above the drusen were strongly correlated with the autofluorescent appearance ($r = 0.78$, $p < 0.001$, and $r = 0.58$, $p < 0.001$, respectively). The strength of correlation with other features appeared less robust: homogeneity ($r = 0.38$; $p = 0.001$), shape ($r = 0.29$; $p = 0.004$), reflectivity ($r = 0.28$; $p = 0.004$) and presence of overlaying foci ($r = 0.25$; $p = 0.12$).

Conclusions: Autofluorescent changes most strongly correlate with drusen size and disruption of the IS-OS layer and may be useful as an additional functional-morphological feature by which drusen and their impact upon overlying photoreceptors may be judged.

PMID: 21757965 [PubMed - as supplied by publisher]

Arch Ophthalmol. 2011 Jul;129(7):885-90.

Psychological and cognitive determinants of vision function in age-related macular degeneration.

Rovner BW, Casten RJ, Massof RW, Leiby BE, Tasman WS.

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OBJECTIVE: To investigate the effect of coping strategies, depression, physical health, and cognition on National Eye Institute Visual Function Questionnaire scores obtained at baseline in a sample of older patients with age-related macular degeneration (AMD) enrolled in the Improving Function in AMD Trial, a randomized controlled clinical trial that compares the efficacy of problem-solving therapy with that of supportive therapy to improve vision function in patients with AMD.

METHODS: Baseline evaluation of 241 older outpatients with advanced AMD who were enrolled in a clinical trial testing the efficacy of a behavioral intervention to improve vision function. Vision function was characterized as an interval-scaled, latent variable of visual ability based on the near-vision subscale of the National Eye Institute Vision Function Questionnaire-25 plus Supplement.

RESULTS: Visual ability was highly correlated with visual acuity. However, a multivariate model revealed that patient coping strategies and cognitive function contributed to their ability to perform near-vision activities independent of visual acuity.

CONCLUSIONS: Patients with AMD vary in their coping strategies and cognitive function and in their visual acuity, and that variability determines patients' self-report of vision function. Understanding patient coping mechanisms and cognition may help increase the precision of vision rating scales and suggest new interventions to improve vision function and quality of life in patients with AMD. Trial Registration clinicaltrials.gov Identifier: NCT00572039.

PMID: 21746979 [PubMed - in process]

Am J Ophthalmol. 2011 Jul 8. [Epub ahead of print]

Diagnostic Evaluation of Type 2 (Classic) Choroidal Neovascularization: Optical Coherence Tomography, Indocyanine Green Angiography, and Fluorescein Angiography.

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PURPOSE: To evaluate the diagnostic characteristics of type 2 (classic) choroidal neovascularizations secondary to age-related macular degeneration using spectral domain-optical coherence tomography (SD OCT), indocyanine green angiography (ICGA), and fluorescein angiography (FA).

DESIGN: Observational case series.

METHODS: setting: Institutional. study population: Thirteen treatment-naïve eyes with type 2 choroidal neovascularization without an occult component. main outcome measures: Greatest horizontal dimension, based on the anatomic features of the neovascular complex by SD OCT (Spectralis), ICGA, and FA; retinal leakage area in late-phase FA and ICGA; and the area of retinal edema in SD OCT. observation procedures: For direct comparison, ICGA and FA images were overlaid manually on infrared plus SD OCT images using VirtualDub and Paint.NET software. Greatest horizontal dimension was measured using Image J software (National Institutes of Health).

RESULTS: The mean greatest horizontal dimension of the neovascular complex and the retinal leakage area consistently were smaller on ICGA compared with the area of retinal edema on SD OCT. According to FA, the greatest horizontal dimension of early, well-demarcated hyperfluorescence was significantly smaller than the neovascular complex on SD OCT. In addition, the greatest horizontal dimension of the retinal leakage area in late-phase FA consistently was smaller than the area of retinal edema on SD OCT.

CONCLUSIONS: In classic choroidal neovascularization, ICGA and FA seem to underestimate the extension of the neovascular complex and the associated retinal pathologic features compared with SD OCT imaging.

PMID: 21742302 [PubMed - as supplied by publisher]

Prog Neurobiol. 2011 Jun 28. [Epub ahead of print]

Age related macular degeneration and drusen: Neuroinflammation in the retina.

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Abstract

Inflammation protects from dangerous stimuli, restoring normal tissue homeostasis. Inflammatory response in the nervous system ("neuroinflammation") has distinct features, which are shared in several diseases. The retina is an immune-privileged site, and the tight balance of immune reaction can be disrupted and lead to age-related macular disease (AMD) and to its peculiar sign, the druse. Excessive activation of inflammatory and immunological cascade with subsequent induction of damage, persistent activation of resident immune cells, accumulation of byproducts that exceeds the normal capacity of clearance giving origin to a chronic local inflammation, alterations in the activation of the complement system, infiltration of macrophages, T-lymphocytes and mast-cells from the bloodstream, participate in the mechanisms which originate the drusen. In addition, aging of the retina and AMD involve also para-inflammation, by which immune cells react to persistent stressful stimuli generating low-grade inflammation, aimed at restoring function and maintaining tissue homeostasis by varying the set point in relation to the new altered conditions. This mechanism is also seen in the normal aging retina, but, in the presence of noxious stimuli as in AMD, it can become chronic and have an adverse outcome. Finally, autophagy may provide new insights to understand AMD pathology, due to its contribution in the removal of defective proteins. Therefore, the AMD retina can represent a valuable model to study neuroinflammation, its mechanisms and therapy in a restricted and controllable environment. Targeting these pathways could represent a new way to treat and prevent both exudative and dry forms of AMD.

PMID: 21740956 [PubMed - as supplied by publisher]

Comput Methods Programs Biomed. 2011 Jul 12. [Epub ahead of print]

Simple methods for segmentation and measurement of diabetic retinopathy lesions in retinal fundus images.

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Abstract

Diabetic retinopathy (DR) is one of the most important complications of diabetes mellitus, which causes serious damages in the retina, consequently visual loss and sometimes blindness if necessary medical treatment is not applied on time. One of the difficulties in this illness is that the patient with diabetes mellitus requires a continuous screening for early detection. So far, numerous methods have been proposed by researchers to automate the detection process of DR in retinal fundus images. In this paper, we developed an alternative simple approach to detect DR. This method was built on the inverse segmentation method, which we suggested before to detect Age Related Macular Degeneration (ARMDs). Background image approach along with inverse segmentation is employed to measure and follow up the degenerations in retinal fundus images. Direct segmentation techniques generate unsatisfactory results in some cases. This is because of the fact that the texture of unhealthy areas such as DR is not homogenous. The inverse method is proposed to exploit the homogeneity of healthy areas rather than dealing with varying structure of unhealthy areas for segmenting bright lesions (hard exudates and cotton wool spots). On the other hand, the background image, dividing the retinal image into high and low intensity areas, is exploited in segmentation of hard exudates and cotton wool spots, and microaneurysms (MAs) and hemorrhages (HEMs), separately. Therefore, a complete segmentation system is developed for segmenting DR, including hard exudates, cotton wool spots, MAs, and HEMs. This application is able to measure total changes across the whole retinal image. Hence, retinal images that belong to the same patients are examined in order to monitor the trend of the illness. To make a comparison with other methods, a Naïve Bayes method is applied for segmentation of DR. The performance of the system, tested on different data sets including various qualities of retinal fundus images, is over 95% in detection of the optic disc (OD), and 90% in segmentation of the DR.

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Biomed Eng Online. 2011 Jul 12;10(1):59. [Epub ahead of print]

Automated Drusen Detection in Retinal Images using Analytical Modelling Algorithms.

Mora AD, Vieira PM, Manivannan A, Fonseca JM.

BACKGROUND: Drusen are common features in the ageing macula associated with exudative Age-Related Macular Degeneration (ARMD). They are visible in retinal images and their quantitative analysis is important in the follow up of the ARMD. However, their evaluation is fastidious and difficult to reproduce when performed manually.

METHODS: This article proposes a methodology for Automatic Drusen Deposits Detection and quantification in Retinal Images (AD3RI) by using digital image processing techniques. It includes an image pre-processing method to correct the uneven illumination and to normalize the intensity contrast with smoothing splines. The drusen detection uses a gradient based segmentation algorithm that isolates drusen and provides basic drusen characterization to the modelling stage. The detected drusen are then fitted by Modified Gaussian functions, producing a model of the image that is used to evaluate the affected area. Twenty two images were graded by eight experts, with the aid of a custom made software and compared with AD3RI. This comparison was based both on the total area and on the pixel-to-pixel analysis. The coefficient of variation, the intraclass correlation coefficient, the sensitivity, the specificity and the kappa coefficient were calculated.

RESULTS: The ground truth used in this study was the experts' average grading. In order to evaluate the proposed methodology three indicators were defined: AD3RI compared to the ground truth (A2G); each expert compared to the other experts (E2E) and a standard Global Threshold method compared to the ground truth (T2G). The results obtained for the three indicators, A2G, E2E and T2G, were: coefficient of variation 28.8 %, 22.5 % and 41.1 %, intraclass correlation coefficient 0.92, 0.88 and 0.67, sensitivity 0.68, 0.67 and 0.74, specificity 0.96, 0.97 and 0.94, and kappa coefficient 0.58, 0.60 and 0.49, respectively.

CONCLUSIONS: The gradings produced by AD3RI obtained an agreement with the ground truth similar to the experts (with a higher reproducibility) and significantly better than the Threshold Method. Despite the higher sensitivity of the Threshold method, explained by its over segmentation bias, it has lower specificity and lower kappa coefficient. Therefore, it can be concluded that AD3RI accurately quantifies drusen, using a reproducible method with benefits for ARMD evaluation and follow-up.

PMID: 21749717 [PubMed - as supplied by publisher]

Aust Fam Physician. 2011 Jul;40(7):529-32.

Nondiabetic retinal pathology - prevalence in diabetic retinopathy screening.

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OBJECTIVE: To determine the prevalence of photographic signs of nondiabetic retinal pathology in Australian general practice patients with diabetes.

METHOD: Three hundred and seven patients with diabetes underwent retinal photography at two general practices, one of which was an indigenous health centre. The images were assessed for signs of pathology by an ophthalmologist.

RESULTS: Signs of nondiabetic retinal pathology were detected in 31% of subjects with adequate photographs. Features suspicious of glaucoma were detected in 7.7% of subjects. Other abnormalities detected included signs of age related macular degeneration (1.9%), epiretinal membranes (2.4%), vascular pathology (9.6%), chorioretinal lesions (2.9%), and congenital disc anomalies (2.9%). Indigenous Australian patients were more likely to have signs of retinal pathology and glaucoma.

CONCLUSION: Signs of nondiabetic retinal pathology were frequently encountered. In high risk groups, general practice based diabetic retinopathy screening may reduce the incidence of preventable visual impairment, beyond the benefits of detection of diabetic retinopathy alone.

PMID: 21743863 [PubMed - in process]

Am J Ophthalmol. 2011 Jul 8. [Epub ahead of print]

Does Laser Still Have a Role in the Management of Retinal Vascular and Neovascular Diseases?

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PURPOSE: To discuss the current role of laser therapies in the management of retinal vascular and neovascular diseases.

METHODS: Laser's role in the management of diabetic retinopathy, age-related macular degeneration, and venous occlusive disease is discussed, with emphasis on comparing laser with anti-vascular endothelial

growth factor (VEGF) therapy and discussion of situations where these treatment methods can be complementary.

RESULTS: Thermal panretinal photocoagulation remains the usual practice for treatment of neovascularization in proliferative diabetic retinopathy and after venous occlusive events. Focal/grid laser still has a role for patients with macular edema resulting from diabetes or venous occlusion that is poorly responsive to anti-VEGF agents and in patients who are unable or unwilling to return for frequent injections. Focal/grid laser also is used as combination therapy with anti-VEGF agents for these indications. Focal laser can be used for extrafoveal choroidal neovascularization to avoid the treatment burden and risks of multiple injections. Photodynamic therapy may be beneficial in the treatment of central serous chorioretinopathy and idiopathic polypoidal choroidal vasculopathy and as combination therapy with anti-VEGF agents in age-related macular degeneration.

CONCLUSIONS: Anti-VEGF agents are effective in preventing vision loss and improving vision in multiple diseases, including diabetic retinopathy, neovascular age-related macular degeneration, and retinal vein occlusions. Despite a substantial decrease in its use for these conditions in recent years, laser therapies continue to serve important roles in our ability to combat retinal pathologic features and will remain a pivotal component of our practices for at least the next several years.

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Genetics

Ophthalmic Genet. 2011 Jul 8. [Epub ahead of print]

Age-related macular degeneration with discordant late stage phenotypes in monozygotic twins.

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Purpose: Age-related macular degeneration (AMD) is a complex disease caused by genetic and environmental factors. Monozygotic twins with late stage AMD provide an opportunity to evaluate the role of environmental factors on a genetically uniform background.

Methods: Monozygosity was determined in four twin pairs by genotyping 15 highly polymorphic tetranucleotide repeat markers. Clinically, the monozygotic twin pairs were evaluated by ophthalmologic examination, fundus autofluorescence (FAF) imaging, and, upon suspicion of choroidal neovascular membranes, by fluorescein angiography. Twin pairs were followed over a period of 4-8 years.

Results: Genetically confirmed monozygotic twins with early stages of AMD reveal striking symmetry of early macular pathology. Upon progression to late stage AMD each twin pair developed a discordant phenotype with respect to disease onset and specific phenotype as choroidal neovascularization (CNV) and geographic atrophy (GA).

Conclusions: Genetic risk variants are known to predispose to the development of AMD. Course and visual outcome of the disease, however, appear to be influenced by environmental factors rather than genetic determinants.

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Ophthalmologica. 2011 Jul 14. [Epub ahead of print]

Genetic Factors Associated with Age-Related Macular Degeneration.

Leveziel N, Tilleul J, Puche N, Zerbib J, Laloum F, Querques G, Souied EH.

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Abstract

Age-related macular degeneration (AMD) is a complex, multifactorial disease associated with environmental and genetic factors. This review emphasizes the clinical impact of the major genetic factors mainly located in the complement factor H gene and on the 10q26 locus, and their current and future implications for the management of AMD.

PMID: 21757876 [PubMed - as supplied by publisher]

PLoS One. 2011;6(7):e21682. Epub 2011 Jul 5.

Therapeutic Action of the Mitochondria-Targeted Antioxidant SkQ1 on Retinopathy in OXYS Rats Linked with Improvement of VEGF and PEDF Gene Expression.

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Abstract

The incidence of age-related macular degeneration (AMD), the main cause of blindness in older patients in the developed countries, is increasing with the ageing population. At present there is no effective treatment for the prevailing geographic atrophy, dry AMD, whereas antiangiogenic therapies successful used in managing the wet form of AMD. Recently we showed that mitochondria-targeted antioxidant plastoquinonyl-decyl-triphenylphosphonium (SkQ1) is able to prevent the development and moreover caused regression of pre-existing signs of the retinopathy in OXYS rats, an animal model of AMD. Here we examine the effects of SkQ1 on expression of key regulators of angiogenesis vascular endothelial growth factor A (VEGF) and its antagonist pigment epithelium-derived factor (PEDF) genes in the retina of OXYS rats as evidenced by real-time PCR and an ELISA test for VEGF using Wistar rats as control. Ophthalmoscopic examinations confirmed that SkQ1 supplementation (from 1.5 to 3 months of age, 250 nmol/kg) prevented development while eye drops SkQ1 (250 nM, from 9 to 12 months) caused some reduction of retinopathy signs in OXYS rats and did not reveal any negative effects on the control Wistar rat's retina. Prevention of premature retinopathy by SkQ1 was connected with an increase of VEGF mRNA and protein in OXYS rat's retina up to the levels corresponding to the Wistar rats, and did not involve changes in PEDF expression. In contrast the treatment with SkQ1 drops caused a decrease of VEGF mRNA and protein levels and an increase in the PEDF mRNA level in the middle-aged OXYS rats, but in Wistar rats the changes of gene expression were the opposite. CONCLUSIONS: The beneficial effects of SkQ1 on retinopathy connected with normalization of expression of VEGF and PEDF in the retina of OXYS rats and depended on age of the animals and the stage of retinopathy.

PMID: 21750722 [PubMed - in process]

Jpn J Ophthalmol. 2011 Jul 9. [Epub ahead of print]

VEGF gene polymorphism and response to intravitreal bevacizumab and triple therapy in age-related macular degeneration.

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PURPOSE: To investigate the association between the vascular endothelial growth factor (VEGF) gene and response to either intravitreal bevacizumab (IVB) or photodynamic therapy with intravitreal triamcinolone acetonide and IVB (triple therapy) for neovascular age-related macular degeneration (AMD).

METHODS: The study consisted of 94 patients with neovascular AMD who underwent IVB and 79 patients with neovascular AMD who underwent triple therapy. Genotypes were determined for four selected tagging single-nucleotide polymorphism (SNP)s of the VEGF gene.

RESULTS: Of the four SNPs studied, one SNP (rs699946) was associated significantly with visual acuity (VA) changes 12 months after treatment-irrespective of whether they received IVB alone ($P = 0.044$) or triple therapy (0.010). Baseline VA was not significantly different among the three genotypes of rs699946 in either treatment group. There were no significant differences in the number of treatments, incidence of recurrence, or the period until the recurrence according to VEGF rs699946 genetic variant.

CONCLUSIONS: The VEGF gene SNP rs699946 was associated with response to IVB alone and to triple therapy in this study. The G allele in SNP rs699946 can thus be applied as a marker for better visual prognosis in patients with neovascular AMD who receive either IVB or triple therapy.

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Invest Ophthalmol Vis Sci. 2011 Jul 8. [Epub ahead of print]

The Effect of Photooxidative Stress and Inflammatory Cytokine on Complement Factor H Expression in Retinal Pigment Epithelial Cells.

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Purpose: Genetic variation in complement factor H (CFH) has been implicated as a major risk factor for age-related macular degeneration (AMD). The reduction in CFH amount or its complement-modulating activity may lead to inadequate control of complement-driven inflammation at outer retina. We explored the effect of photooxidative stress and inflammatory cytokine on the expression of CFH in retinal pigment epithelial (RPE) cells.

Methods: Cultured human RPE cells were exposed to blue light in the presence of interferon- γ (IFN- γ). CFH expression in cell lysate was examined by Western blot and the secretory CFH in culture medium was analyzed by ELISA. RPE cells were treated with vitamin C and Tempol before photooxidative treatments. The intracellular reactive oxygen species were examined by flow cytometry.

Results: IFN- γ increased CFH expression in RPE and the expression was suppressed significantly under concomitant blue light illumination. The secretory CFH level also decreased significantly under blue light illumination, which was related to the decreased intracellular mRNA and protein expressions of CFH. The suppression was mediated through oxidative mechanism, and was particularly related to superoxide anion generation. The suppression of CFH expression in RPE under blue light illumination was abrogated by vitamin C and Tempol.

Conclusions: Photooxidative stress reduces the ability of IFN- γ to increase CFH expression in RPE. Apart from reducing the oxidative damage, vitamin C reduces the suppression of CFH under photooxidative stress. These results suggest a new perspective of the interaction between oxidative stress and inflammation, and provide a potential novel treatment strategy for AMD.

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Diet

Annu Rev Nutr. 2011 Aug 21;31:321-51.

Docosahexaenoic Acid signalolipidomics in nutrition: significance in aging, neuroinflammation, macular degeneration, Alzheimer's, and other neurodegenerative diseases.

Bazan NG, Molina MF, Gordon WC.

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Abstract

Essential polyunsaturated fatty acids (PUFAs) are critical nutritional lipids that must be obtained from the diet to sustain homeostasis. Omega-3 and -6 PUFAs are key components of biomembranes and play important roles in cell integrity, development, maintenance, and function. The essential omega-3 fatty acid family member docosahexaenoic acid (DHA) is avidly retained and uniquely concentrated in the nervous system, particularly in photoreceptors and synaptic membranes. DHA plays a key role in vision, neuroprotection, successful aging, memory, and other functions. In addition, DHA displays anti-inflammatory and inflammatory resolving properties in contrast to the proinflammatory actions of several members of the omega-6 PUFAs family. This review discusses DHA signalolipidomics, comprising the cellular/tissue organization of DHA uptake, its distribution among cellular compartments, the organization and function of membrane domains rich in DHA-containing phospholipids, and the cellular and molecular events revealed by the uncovering of signaling pathways regulated by DHA and docosanoids, the DHA-derived bioactive lipids, which include neuroprotectin D1 (NPD1), a novel DHA-derived stereoselective mediator. NPD1 synthesis agonists include neurotrophins and oxidative stress; NPD1 elicits potent anti-inflammatory actions and pro-homeostatic bioactivity, is anti-angiogenic, promotes corneal nerve regeneration, and induces cell survival. In the context of DHA signalolipidomics, this review highlights aging and the evolving studies on the significance of DHA in Alzheimer's disease, macular degeneration, Parkinson's disease, and other brain disorders. DHA signalolipidomics in the nervous system offers emerging targets for pharmaceutical intervention and clinical translation.

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