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Drug treatment

Ocul Surf. 2011 Oct;9(4):227-37.

Anti-VEGF Treatment of Corneal Neovascularization.

Keating AM, Jacobs DS.

From the Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston.

Abstract

Vascular endothelial growth factor (VEGF) is an angiogenic factor shown to be a critical secreted cytokine in tumorigenesis and retinal neovascularization (NV). Currently, there are two anti-VEGF agents, pegaptanib and ranizumab, approved by the United States Food and Drug Administration (FDA) for intravitreal use in the treatment of wet age-related macular degeneration (AMD). Bevacizumab is FDA-approved for intravenous administration in the treatment of several cancers and is in widespread use, off-label, as an intravitreal injection to treat a variety of retinal pathologies. Animal studies demonstrate the role of VEGF in corneal NV. There are now a number of human case series reporting the use of anti-VEGF agents, primarily bevacizumab, to treat corneal NV. This review summarizes reports to date on the use of anti-VEGF agents in the treatment of corneal NV in humans, noting the limitations of current data and the need for further studies. The experience of one clinician with the use of an anti-VEGF drug in the treatment of active corneal NV is presented.

PMID: 22023817 [PubMed - in process]

Farm Hosp. 2011 Oct 24. [Epub ahead of print]

New drugs for indications currently treated by off-label drugs: intravitreal dexamethasone and ranibizumab.

[Article in English, Spanish]

Monzón Moreno A.

Servicio de Farmacia, Hospital Virgen Macarena, Sevilla, España.

PMID: 22030162 [PubMed - as supplied by publisher]

J Fr Ophtalmol. 2011 Oct 25. [Epub ahead of print]

[Bevacizumab versus ranibizumab: A draw?]

[Article in French]

Souied EH, Cohen SY, Kodjikian L.

Service d'ophtalmologie, hôpital intercommunal de Créteil, université Paris-Est Créteil, 40, avenue de Verdun, 94000 Créteil, France.

PMID: 22033297 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Mol Vis. 2011;17:2580-95. Epub 2011 Oct 5.

RPE and neuronal differentiation of allotransplantated porcine ciliary epithelium-derived cells.

Guduric-Fuchs J, Chen W, Price H, Archer DB, Cogliati T.

PURPOSE: Cell replacement has the potential to be applied as a therapeutic strategy in retinal degenerative diseases such as retinitis pigmentosa and age-related macular degeneration (AMD) for which no adequate pharmacological and surgical treatments are currently available. Although controversial, the use of ciliary epithelium (CE)-derived cells is supported by evidence showing their differentiation into retinal phenotypes. This study examines the differentiation potential of porcine CE-derived cells in vitro and their survival, migration, morphological characteristics, and immunohistochemical phenotype in vivo, upon transplantation into the subretinal space of normal pigs.

METHODS: Cells were isolated from the CE of postnatal pigs and were grown in a suspension sphere culture. Differentiation was assessed in vitro after exposure to laminin and the addition of serum. For transplantation, CE-derived spheres were dissociated, labeled with CM-DiI vital dye, and the cells were injected subretinally into one eye of eight week-old allorecipients. The eyes were examined at eight days and at two and four weeks after transplantation.

RESULTS: Cells positive for neuronal and retinal pigment epithelium (RPE) markers were detected by immunohistochemistry in differentiation cultures. Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) revealed upregulation of neuronal markers after in vitro differentiation. CM-DiI dye-labeled CE-derived cells dissociated from primary spheres survived for up to four weeks after transplantation in vivo. Some of the surviving cells migrated distantly from the injection site. Large clusters of transplanted cells integrated into the RPE layer and multilayered RPE-like structures positive for RPE65 were often observed. Grafted cells were also identified in the neuroretina where 5%-10% were positive for recoverin, protein kinase C alpha (PKCα), and calbindin.

CONCLUSIONS: The efficient conversion to an RPE-like phenotype suggests that CE-derived cells could be a potential source of RPE for cell replacement. Our data also suggest that the ability of these cells to acquire neuronal phenotypes is influenced by the environment. Thus, pre-differentiated or (re)programmed CE-derived cells may be more amenable for retinal repair.

PMID: 22025893 [PubMed - in process] PMCID: PMC3198501

J Biomed Opt. 2011 Oct;16(10):106013.

Using ultrahigh sensitive optical microangiography to achieve comprehensive depth resolved microvasculature mapping for human retina.

An L, Shen TT, Wang RK.

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Abstract

This paper presents comprehensive and depth-resolved retinal microvasculature images within human retina achieved by a newly developed ultrahigh sensitive optical microangiography (UHS-OMAG) system. Due to its high flow sensitivity, UHS-OMAG is much more sensitive to tissue motion due to the involuntary movement of the human eye and head compared to the traditional OMAG system. To mitigate these motion artifacts on final imaging results, we propose a new phase compensation algorithm in which the traditional phase-compensation algorithm is repeatedly used to efficiently minimize the motion artifacts. Comparatively, this new algorithm demonstrates at least 8 to 25 times higher motion tolerability, critical for the UHS-OMAG system to achieve retinal microvasculature images with high quality. Furthermore, the new UHS-OMAG system employs a high speed line scan CMOS camera (240 kHz A-line scan rate) to capture 500 A-lines for one B-frame at a 400 Hz frame rate. With this system, we performed a series of in vivo experiments to visualize the retinal microvasculature in humans. Two featured imaging protocols are utilized. The first is of the low lateral resolution (16 μm) and a wide field of view (4 × 3 mm(2) with single scan and 7 × 8 mm(2) for multiple scans), while the second is of the high lateral resolution (5 μm) and a narrow field of view (1.5 × 1.2 mm(2) with single scan). The great imaging performance delivered by our system suggests that UHS-OMAG can be a promising noninvasive alternative to the current clinical retinal microvasculature imaging techniques for the diagnosis of eye diseases with significant vascular involvement, such as diabetic retinopathy and age-related macular degeneration.

PMID: 22029360 [PubMed - in process]

PLoS One. 2011;6(10):e26154. Epub 2011 Oct 12.

Illusory Contours over Pathological Retinal Scotomas.

De Stefani E, Pinello L, Campana G, Mazzarolo M, Lo Giudice G, Casco C.

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Abstract

Our visual percepts are not fully determined by physical stimulus inputs. Thus, in visual illusions such as the Kanizsa figure, inducers presented at the corners allow one to perceive the bounding contours of the figure in the absence of luminance-defined borders. We examined the discrimination of the curvature of these illusory contours that pass across retinal scotomas caused by macular degeneration. In contrast with previous studies with normal-sighted subjects that showed no perception of these illusory contours in the region of physiological scotomas at the optic nerve head, we demonstrated perfect discrimination of the curvature of the illusory contours over the pathological retinal scotoma. The illusion occurred despite the large scar around the macular lesion, strongly reducing discrimination of whether the inducer openings were acute or obtuse and suggesting that the coarse information in the inducers (low spatial frequency) sufficed. The result that subjective contours can pass through the pathological retinal scotoma suggests that the visual cortex, despite the loss of bottom-up input, can use low-spatial frequency information from the inducers to form a neural representation of new complex geometrical shapes inside the scotoma.

PMID: 22022546 [PubMed - in process] PMCID: PMC3192156

Retina. 2011 Nov;31(10):2123-4.

Gas-assisted release of vitreomacular adhesion in wet age-related macular degeneration.

Kim YM, Lee SJ, Koh HJ.

From the *The Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, Seoul, Korea; and †Department of Ophthalmology, Dongguk University Ilsan Hospital, Dongguk University, Seoul, Korea.

PMID: 22027799 [PubMed - in process]

Am J Ophthalmol. 2011 Oct 24. [Epub ahead of print]

Quantitative Imaging of Retinal Pigment Epithelial Detachments Using Spectral-Domain Optical Coherence Tomography.

Penha FM, Rosenfeld PJ, Gregori G, Falcão M, Yehoshua Z, Wang F, Feuer WJ.

Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida.

PURPOSE: To evaluate the reproducibility of area and volume measurements of retinal pigment epithelium detachments (PEDs) in eyes of patients with age-related macular degeneration using spectral-domain optical coherence tomography imaging and a novel automated, quantitative algorithm.

DESIGN: Prospective study to evaluate a diagnostic technology.

METHODS: Patients with PEDs associated with age-related macular degeneration underwent spectral-domain optical coherence tomography imaging. Each eye was imaged 5 times, and each scan consisted of a raster pattern comprising 40 000 uniformly spaced A-scans organized as a 200 × 200 A-scan array. Each raster scan covered a retinal area of 6 × 6 mm encompassing the entire PED. A novel algorithm was used to create PED maps that permitted both qualitative and quantitative assessment of PED area and volume. Test-retest standard deviations of PED area and volume measurements were calculated for each eye.

RESULTS: Sixty-three eyes of 58 patients were enrolled in this study. The qualitative appearance and the quantitative measurements of PED area and volume were highly reproducible over the 5 different datasets obtained from each eye. The intraclass correlation coefficient was more than 0.99 for both area and volume measurements obtained using the entire dataset.

CONCLUSIONS: A novel algorithm for the qualitative and quantitative assessment of PEDs imaged using spectral-domain optical coherence tomography was shown to be highly reproducible. The ability to measure PED area and volume reliably represents a novel strategy for following disease progression, especially when assessing the response of vascularized PEDs to antiangiogenic therapy.

PMID: 22030354 [PubMed - as supplied by publisher]

Methods Mol Biol. 2011;807:179-218.

Adeno-associated virus mediated gene therapy for retinal degenerative diseases.

Stieger K, Cronin T, Bennett J, Rolling F.

Department of Ophthalmology, Justus-Liebig-University Giessen, Gissen, Germany.

Abstract

Retinal gene therapy holds great promise for the treatment of inherited and noninherited blinding diseases such as retinitis pigmentosa and age-related macular degeneration. The most widely used vectors for ocular gene delivery are based on adeno-associated virus (AAV) because it mediates long-term transgene expression in a variety of retinal cell types and elicits minimal immune responses. Inherited retinal diseases are nonlethal and have a wide level of genetic heterogeneity. Many of the genes have now been identified and their function elucidated, providing a major step towards the development of gene-based treatments. Extensive preclinical evaluation of gene transfer strategies in small and large animal models is key to the development of successful gene-based therapies for the retina. These preclinical studies have already allowed the field to reach the point where gene therapy to treat inherited blindness has been brought to clinical trial.In this chapter, we focus on AAV-mediated specific gene therapy for inherited retinal degenerative diseases, describing the disease targets, the preclinical studies in animal models and the recent success of the LCA-RPE65 clinical trials.

PMID: 22034031 [PubMed - in process]

Graefes Arch Clin Exp Ophthalmol. 2011 Oct 28. [Epub ahead of print]

Intra and interobserver agreement in the classification of fundus autofluorescence patterns in geographic atrophy secondary to age-related macular degeneration.

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BACKGROUND: To describe the intra and interobserver agreement in the evaluation of fundus autofluorescence patterns in geographic atrophy secondary to age-related macular degeneration.

METHODS: A consecutive series of patients with geographic atrophy and fundus autofluorescence images of a minimum acceptable quality for grading were included. Four observers with experience in the evaluation of autofluorescence images independently classified the randomly presented series of images on two occasions, at least 1 month apart from each other (intraobserver analysis). The second determination of each observer was used for evaluation of interobserver agreement. The kappa statistic and 95% confidence intervals, together with percentages of agreement, were used to analyze the results.

RESULTS: The final sample included 69 eyes of 49 patients. Intraobserver agreement ranged from substantial to almost perfect (kappa between 0.51 and 0.83), while interobserver results ranged from poor to substantial (corresponding to kappa between 0.30 and 0.62). The use of more simple classifications improved reproducibility.

CONCLUSIONS: Although intraobserver reproducibility was high, interobserver agreement was variable. Clear descriptions and a uniform set of criteria to classify these patients are needed if fundus autofluorescence imaging is used to evaluate patients with geographic atrophy.

PMID: 22033626 [PubMed - as supplied by publisher]

Pathogenesis

Retina. 2011 Oct 25. [Epub ahead of print]

SERUM PARAOXONASE PHENOTYPE DISTRIBUTION IN EXUDATIVE AGE-RELATED MACULAR DEGENERATION AND ITS RELATIONSHIP TO HOMOCYSTEINE AND OXIDIZED LOW-DENSITY LIPOPROTEIN.

Javadzadeh A, Ghorbanihaghjo A, Bahreini E, Rashtchizadeh N, Argani H, Alizadeh S.

From the Biotechnology Research Center and †Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

PURPOSE: Disequilibrium between oxidative stress and antioxidant levels has been proposed as an important case of exudative age-related macular degeneration (AMD). The aim of the present study was to investigate homocysteine (Hcy) level and antioxidant paraoxonase 1 (PON1) activity within its phenotypes together with oxidized low-density lipoprotein (OX-LDL) levels in the patients with exudative AMD.

METHODS: Serum PON1 activity and plasma Hcy and OX-LDL levels were analyzed in 45 exudative AMD patients and compared with 45 healthy controls. Paraoxonase 1 activity was measured in serum using paraoxon and phenylacetate as substrates. The PON1 phenotype was determined using double-substrate method. Homocysteine and OX-LDL levels were determined by enzyme-linked immunosorbent assay method.

RESULTS: The distribution of PON1 phenotypes was significantly different between the patients with exudative AMD and control subjects (chi-square = 6.17, P = 0.01). AA phenotype with low activity was significantly more frequent in exudative AMD patients compared with healthy subjects (62.2% vs. 35.6%, respectively). Other phenotype frequencies in the patients compared with controls were as AB phenotype (intermediate activity) 28.9% versus 46.7% and BB phenotype (high activity) 8.9% versus 17.8%, respectively. Except in BB phenotype (P = 0.2), patients with AA and AB phenotypes had higher plasma Hcy levels in comparison to those of controls (P = 0.02 and P = 0.03, respectively). The mean OX-LDL levels, in all 3 phenotypes (P < 0.05), and OX-LDL/high-density lipoprotein ratio, in AA and AB phenotypes (P = 0.001, P = 0.1, respectively) but not in BB (P = 0.1), were significantly higher in the patients than controls. No significant differences in comparison of Hcy and OX-LDL levels between 3 PON1 phenotypes in both control (P = 0.6 for Hcy, P = 0.7 for OX-LDL) and patients (P = 0.8 for Hcy, P = 0.6 for OX-LDL) were found

CONCLUSION: Increased plasma OX-LDL levels and ratios of OX-LDL/high-density lipoprotein, as biomarkers of lipoprotein oxidative stress, higher levels of Hcy, as oxidant agent, and more common low or intermediate PON1 activity in patients with exudative AMD, compared with controls, indicate that PON1 activity is insufficient to explain the increased oxidative stress observed in exudative AMD.

PMID: 22030834 [PubMed - as supplied by publisher]

Genetics

PLoS One. 2011;6(10):e25598. Epub 2011 Oct 12.

A 32 kb Critical Region Excluding Y402H in CFH Mediates Risk for Age-Related Macular Degeneration.

Sivakumaran TA, Igo RP Jr, Kidd JM, Itsara A, Kopplin LJ, Chen W, Hagstrom SA, Peachey NS, Francis PJ, Klein ML, Chew EY, Ramprasad VL, Tay WT, Mitchell P, Seielstad M, Stambolian DE, Edwards AO, Lee KE, Leontiev DV, Jun G, Wang Y, Tian L, Qiu F, Henning AK, Laframboise T, Sen P, Aarthi M, George R, Raman R, Das MK, Vijaya L, Kumaramanickavel G, Wong TY, Swaroop A, Abecasis GR, Klein R, Klein BE, Nickerson DA, Eichler EE, Iyengar SK.

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Abstract

Complement factor H shows very strong association with Age-related Macular Degeneration (AMD), and recent data suggest that multiple causal variants are associated with disease. To refine the location of the disease associated variants, we characterized in detail the structural variation at CFH and its paralogs, including two copy number polymorphisms (CNP), CNP147 and CNP148, and several rare deletions and du-

plications. Examination of 34 AMD-enriched extended families (N=293) and AMD cases (White N=4210 Indian=134; Malay=140) and controls (White N=3229; Indian=117; Malay=2390) demonstrated that deletion CNP148 was protective against AMD, independent of SNPs at CFH. Regression analysis of seven common haplotypes showed three haplotypes, H1, H6 and H7, as conferring risk for AMD development. Being the most common haplotype H1 confers the greatest risk by increasing the odds of AMD by 2.75-fold (95% CI=[2.51, 3.01]; p=8.31×10(-109)); Caucasian (H6) and Indian-specific (H7) recombinant haplotypes increase the odds of AMD by 1.85-fold (p=3.52×10(-9)) and by 15.57-fold (P=0.007), respectively. We identified a 32-kb region downstream of Y402H (rs1061170), shared by all three risk haplotypes, suggesting that this region may be critical for AMD development. Further analysis showed that two SNPs within the 32 kb block, rs1329428 and rs203687, optimally explain disease association. rs1329428 resides in 20 kb unique sequence block, but rs203687 resides in a 12 kb block that is 89% similar to a noncoding region contained in ΔCNP148. We conclude that causal variation in this region potentially encompasses both regulatory effects at single markers and copy number.

PMID: 22022419 [PubMed - in process] PMCID: PMC3192039

Nat Genet. 2011 Oct 23. doi: 10.1038/ng.976. [Epub ahead of print]

A rare penetrant mutation in CFH confers high risk of age-related macular degeneration.

Raychaudhuri S, Iartchouk O, Chin K, Tan PL, Tai AK, Ripke S, Gowrisankar S, Vemuri S, Montgomery K, Yu Y, Reynolds R, Zack DJ, Campochiaro B, Campochiaro P, Katsanis N, Daly MJ, Seddon JM.

1] Division of Genetics, Brigham and Women's Hospital, Boston, Massachusetts, USA. [2] Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Boston, Massachusetts, USA. [3] Partners HealthCare Center for Personalized Genetic Medicine, Boston, Massachusetts, USA. [4] Program in Medical and Population Genetics, Broad Institute, Cambridge, Massachusetts, USA.

Abstract

Two common variants in the gene encoding complement factor H (CFH), the Y402H substitution (rs1061170, c.1204C>T) and the intronic rs1410996 SNP, explain 17% of age-related macular degeneration (AMD) liability. However, proof for the involvement of CFH, as opposed to a neighboring transcript, and knowledge of the potential mechanism of susceptibility alleles are lacking. Assuming that rare functional variants might provide mechanistic insights, we used genotype data and high-throughput sequencing to discover a rare, high-risk CFH haplotype with a c.3628C>T mutation that resulted in an R1210C substitution. This allele has been implicated previously in atypical hemolytic uremic syndrome, and it abrogates C-terminal ligand binding. Genotyping R1210C in 2,423 AMD cases and 1,122 controls demonstrated high penetrance (present in 40 cases versus 1 control, P = 7.0 × 10(-6)) and an association with a 6-year-earlier onset of disease (P = 2.3 × 10(-6)). This result suggests that loss-of-function alleles at CFH are likely to drive AMD risk. This finding represents one of the first instances in which a common complex disease variant has led to the discovery of a rare penetrant mutation.

PMID: 22019782 [PubMed - as supplied by publisher]

Hum Hered. 2011 Oct 19;72(2):142-152. [Epub ahead of print]

Comparison of Six Statistics of Genetic Association Regarding Their Ability to Discriminate between Causal Variants and Genetically Linked Markers.

Lorenzo Bermejo J, Garcia Perez A, Brandt A, Hemminki K, Matthews AG.

Institute of Medical Biometry and Informatics, University Hospital Heidelberg, INF 305, Heidelberg, Germany.

Objectives: Genome-wide association (GWA) studies still rely on the common-disease common-variant hypothesis since the assumption is associated with increased power. In GWA studies, polymorphisms are genotyped and their association with disease is investigated. Most of the identified associations are indirect and reflect a shared inheritance of the genotyped markers and genetically linked causal variants. We have compared six statistics of genetic association regarding their ability to discriminate between markers and causal susceptibility variants, including a probability value (Pval) and a Bayes Factor (BF) based on logistic regression, and the attributable familial relative risk (FRR).

Methods: We carried out a simulation-based sensitivity analysis to explore several conceivable scenarios. Theoretical results were illustrated by established causal associations with age-related macular degeneration and by using imputed data based on HapMap for a case-control study of breast cancer.

Results: Our data indicate that a representation of genetic association by FRRs and BFs generally facilitates the distinction of causal variants. The FRR showed the best discriminative power under most investigated scenarios, but no single statistic outperformed the others in all situations. For example, rare moderate- to low-penetrance variants (allele frequency: 1%, dominant odds ratio: ≤2.0) seem to be best discriminated by BFs.

Conclusions: Present results may help to fully utilize the data generated in association studies that take advantage of next generation sequencing and/or multiple imputation based on the 1000 Genomes Project.

PMID: 22025134 [PubMed - as supplied by publisher]

Immunobiology. 2011 Oct 5. [Epub ahead of print]

Genetic variation in complement regulators and susceptibility to age-related macular degeneration.

Cipriani V, Matharu BK, Khan JC, Shahid H, Stanton CM, Hayward C, Wright AF, Bunce C, Clayton DG, Moore AT, Yates JR.

Institute of Ophthalmology, University College London, UK; Moorfields Eye Hospital, London, UK.

OBJECTIVES: Age-related macular degeneration (AMD) is the commonest cause of blindness in Western populations. Risk is influenced by age, genetic and environmental factors. Complement activation appears to be important in the pathogenesis and associations have been found between AMD and genetic variations in complement regulators such as complement factor H. We therefore investigated other complement regulators for association with AMD.

METHODS: We carried out a case-control study to test for association between AMD and single nucleotide polymorphisms (SNPs) spanning the genes encoding complement factor P (CFP, properdin), CD46 (membrane cofactor protein, MCP), CD55 (decay accelerating factor, DAF) and CD59 (protectin). All cases and controls were examined by an ophthalmologist and had independent grading of fundus photographs to confirm their disease status.

RESULTS: 20 SNPs were genotyped in 446 cases and 262 controls. For two SNPs with p-values approaching significance additional subjects were genotyped to increase the numbers to 622 cases and 359 controls. There was no evidence of association between AMD and any of the SNPs typed in CFP, CD46, CD55 or CD59.

CONCLUSIONS: In a case-control sample that has shown the well established associations between AMD and variants in CFH, CFB and C3 there was absence of association with SNPs in CFP, CD46, CD55 and CD59. This suggests that these are not important susceptibility genes for AMD.

PMID: 22024702 [PubMed - as supplied by publisher]

Curr Eye Res. 2011 Oct 26. [Epub ahead of print]

Lack of Association with PEDF Met72Thr Variant in Neovascular Age-related Macular Degeneration and Polypoidal Choroidal Vasculopathy in a Han Chinese Population.

Wu K, Wen F, Zuo C, Li M, Zhang X, Chen H, Zeng R.

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University , Guangzhou , China.

Purpose: To investigate whether Met72Thr (rs1136287), a common single nucleotide polymorphism (SNP) variant of the pigment epithelium-derived factor (PEDF) gene, is associated with neovascular age-related macular degeneration (nAMD) or polypoidal choroidal vasculopathy (PCV) in a Han Chinese cohort. Methods: We genotyped Met72Thr (rs1136287) in persons of Han Chinese descent: 177 PCV patients, 131 nAMD patients, and 182 control persons. Genotyping was accomplished using the Multiplex SNaPshot system and by direct DNA sequencing. Genotypes and allele frequencies of patients and controls were evaluated for the SNP using PLINK software. Results: The minor allele frequency of the PEDF Met72Thr variant did not differ significantly between either PCV or nAMD and the control group: p = 0.3822 and p = 0.9822, respectively. The p-values for the additive, dominant, and recessive models were not statistically significant for PCV or nAMD. Conclusions: No evidence was found to support a role for the Met72Thr variant in susceptibility to either PCV or nAMD in a Han Chinese cohort.

PMID: 22029535 [PubMed - as supplied by publisher]

Diet

Optometry. 2011 Nov;82(11):667-680.e6.

Randomized, double-blind, placebo-controlled study of zeaxanthin and visual function in patients with atrophic age-related macular degeneration The Zeaxanthin and Visual Function Study (ZVF) FDA IND #78, 973.

Richer SP, Stiles W, Graham-Hoffman K, Levin M, Ruskin D, Wrobel J, Park DW, Thomas C.

Captain James A. Lovell Federal Health Care Facility, North Chicago, Illinois; Rosalind Franklin University of Medicine and Science, Chicago Medical School, North Chicago, Illinois.

BACKGROUND: The purpose of this study is to evaluate whether dietary supplementation with the carotenoid zeaxanthin (Zx) raises macula pigment optical density (MPOD) and has unique visual benefits for patients with early atrophic macular degeneration having visual symptoms but lower-risk National Institute of Health/National Eye Institute/Age-Related Eye Disease Study characteristics.

METHODS: This was a 1-year, n = 60 (57 men, 3 women), 4-visit, intention-to-treat, prospective, randomized controlled clinical trial of patients (74.9 years, standard deviation [SD] 10) with mild-to-moderate age-related macular degeneration (AMD) randomly assigned to 1 of 2 dietary supplement carotenoid pigment intervention groups: 8 mg Zx (n = 25) and 8 mg Zx plus 9 mg lutein (L) (n = 25) or 9 mg L ("Faux Placebo," control group, n = 10). Analysis was by Bartlett's test for equal variance, 3-way repeated factors analysis of variance, independent t test (P < 0.05) for variance and between/within group differences, and post-hoc Scheffé's tests. Estimated foveal heterochromic flicker photometry, 1° macular pigment optical density (MPOD QuantifEye(®)), low- and high-contrast visual acuity, foveal shape discrimination (Retina Foundation of the Southwest), 10° yellow kinetic visual fields (KVF), glare recovery, contrast sensitivity function (CSF), and 6° blue cone ChromaTest(®) color thresholds were obtained serially at 4, 8, and 12 months.

RESULTS: Ninety percent of subjects completed ≥ 2 visits with an initial Age-Related Eye Disease Study report #18 retinopathy score of 1.4 (1.0 SD)/4.0 and pill intake compliance of 96% with no adverse effects. There were no intergroup differences in 3 major AMD risk factors: age, smoking, and body mass index as

well as disease duration and Visual Function Questionnaire 25 composite score differences. Randomization resulted in equal MPOD variance and MPOD increasing in each of the 3 groups from 0.33 density units (du) (0.17 SD) baseline to 0.51 du (0.18 SD) at 12 m, (P = 0.03), but no between-group differences (Analysis of Variance; P = 0.47). In the Zx group, detailed high-contrast visual acuity improved by 1.5 lines, Retina Foundation of the Southwest shape discrimination sharpened from 0.97 to 0.57 (P = 0.06, 1-tail), and a larger percentage of Zx patients experienced clearing of their KVF central scotomas (P = 0.057). The "Faux Placebo" L group was superior in terms of low-contrast visual acuity, CSF, and glare recovery, whereas Zx showed a trend toward significance.

CONCLUSION: In older male patients with AMD, Zx-induced foveal MPOD elevation mirrored that of L and provided complementary distinct visual benefits by improving foveal cone-based visual parameters, whereas L enhanced those parameters associated with gross detailed rod-based vision, with considerable overlap between the 2 carotenoids. The equally dosed (atypical dietary ratio) Zx plus L group fared worse in terms of raising MPOD, presumably because of duodenal, hepatic-lipoprotein or retinal carotenoid competition. These results make biological sense based on retinal distribution and Zx foveal predominance.

PMID: 22027699 [PubMed - in process]