

Issue 92

Tuesday August 7, 2012

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

PLoS One. 2012;7(7):e42014. Epub 2012 Jul 25.

Impact of Loading Phase, Initial Response and CFH Genotype on the Long-Term Outcome of Treatment for Neovascular Age-Related Macular Degeneration.

Menghini M, Kloeckener-Gruissem B, Fleischhauer J, Kurz-Levin MM, Sutter FK, Berger W, Barthelmes D.

Department of Ophthalmology, University Hospital of Zurich, Zurich, Switzerland.

OBJECTIVE: Factors influencing the outcome of anti-VEGF treatment in neovascular AMD are still investigated. We analyzed the impact of a loading phase, the significance of an initial response for the long-term and the effect of the CFH polymorphism (p.His402Tyr) on treatment outcome.

METHODS: Patients treated with ranibizumab for neovascular AMD were analyzed over a period of 24 months by assessing effects of loading phase, initial response and genotype of CFH rs1061170 (c.1204C>T, p.His402Tyr).

RESULTS: 204 eyes were included. A change of +5.0 [-1;+11] letters and +1.5 [-5.5;+9.5] was observed with a median of 4 [3]; [7] and 10 [7]; [14] ranibizumab injections during 12 and 24 months, respectively. Loading phase was no significant predictor for treatment as VA outcome in eyes with and without loading phase was similar ($p=0.846$ and $p=0.729$) at 12 and 24 months. In contrast, initial response was a significant predictor for improving vision of 5 or more letters at 12 ($p=0.001$; OR=6.75) and 24 months ($p=0.01$; OR=4.66). Furthermore, the CT genotype at CFH rs1061170 was identified as a significant predictor for a favorable VA outcome at 12 and 24 months (OR=6.75, $p=0.001$ and OR=4.66, $p=0.01$).

CONCLUSIONS: Our data suggest that clinical decisions regarding treatment may be guided by observing patients' initial response as well as their genotype of SNP rs1061170, while the criterion of loading phase may not bear the customary value.

PMID: 22848690 [PubMed - in process] PMCID: PMC3405003 Free PMC Article

Ophthalmology. 2012 Jul 26. [Epub ahead of print]

Cumulative Effect of Risk Alleles in CFH, ARMS2, and VEGFA on the Response to Ranibizumab Treatment in Age-Related Macular Degeneration.

Smailhodzic D, Muether PS, Chen J, Kwestro A, Zhang AY, Omar A, Van de Ven JP, Keunen JE, Kirchhof

B, Hoyng CB, Klevering BJ, Koenekoop RK, Fauser S, den Hollander AI.

Department of Ophthalmology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands.

PURPOSE: Intravitreal ranibizumab injections currently are the standard treatment for neovascular age-related macular degeneration (AMD). However, a broad range of response rates have been observed, the reasons for which are poorly understood. This pharmacogenetic study evaluated the impact of high-risk alleles in CFH, ARMS2, VEGFA, vascular endothelial growth factor (VEGF) receptor KDR, and genes involved in angiogenesis (LRP5, FZD4) on the response to ranibizumab treatment and on the age of treatment onset. In contrast to previous studies, the data were stratified according to the number of high-risk alleles to enable the study of the combined effects of these genotypes on the treatment response.

DESIGN: Case series study.

PARTICIPANTS: A cohort of 420 eyes of 397 neovascular AMD patients.

METHODS: The change in visual acuity (VA) between baseline and after 3 ranibizumab injections was calculated. Genotyping of single nucleotide polymorphisms in the CFH, ARMS2, VEGFA, KDR, LRP5, and FZD4 genes was performed. Associations were assessed using linear mixed models.

MAIN OUTCOME MEASURES: The VA change after 3 ranibizumab injections and the age of neovascular disease onset.

RESULTS: After ranibizumab treatment, AMD patients without risk alleles in the CFH and ARMS2 genes (4.8%) demonstrated a mean VA improvement of 10 Early Treatment Diabetic Retinopathy Study (ETDRS) letters, whereas no VA improvement was observed in AMD patients with 4 CFH and ARMS2 risk alleles (6.9%; $P = 0.014$). Patients with 4 high-risk alleles in CFH and ARMS2 were 5.2 years younger than patients with 1 or 2 risk alleles, respectively (63.5%; $P < 0.0001$). The mean age at which the first ranibizumab treatment was carried out among AMD patients with all 6 risk alleles in CFH, ARMS2, and VEGFA was 65.9 years (2%) versus 75.3 years in patients with 0 or 1 high-risk allele (8.8%; $P = 0.001$). After ranibizumab treatment, patients with 6 high-risk alleles demonstrated a mean VA loss of 10 ETDRS letters ($P < 0.0001$).

CONCLUSIONS: This study evaluated the largest pharmacogenetic AMD cohort reported to date. A cumulative effect of high-risk alleles in CFH, ARMS2, and VEGFA seems to be associated with a younger age of onset in combination with poor response rates to ranibizumab treatment.

PMID: 22840423 [PubMed - as supplied by publisher]

Retina. 2012 Jul 27. [Epub ahead of print]

RETINAL PIGMENT EPITHELIAL ATROPHY IN PATIENTS WITH EXUDATIVE AGE-RELATED MACULAR DEGENERATION UNDERGOING ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY.

Lois N, McBain V, Abdelkader E, Scott NW, Kumari R.

*Department of Ophthalmology, Grampian University Hospital-NHS Trust, Aberdeen, Scotland, United Kingdom †Medical Statistics Team, Division of Applied Health Sciences, University of Aberdeen, Aberdeen, Scotland, United Kingdom.

PURPOSE: To evaluate the occurrence of retinal pigment epithelial atrophy in patients with age-related macular degeneration undergoing anti-vascular endothelial growth factor therapy.

METHODS: The study is a retrospective review. Eligible were patients with age-related macular degeneration and choroidal neovascular membranes treated with anti-vascular endothelial growth factor between October 2007 and February 2011; they were followed for >3 months, with fundus photographs and

fluorescein angiography at baseline and with autofluorescence and near-infrared autofluorescence images at baseline and follow-up. Demographics, visual acuity, the type of choroidal neovascular membranes, the number of treatments performed, and the length of follow-up were recorded. Autofluorescence and near-infrared autofluorescence images were evaluated for the presence or absence of areas of reduced signal. A multilevel logistic regression model was used to investigate the factors that may be associated with "progression of atrophy" at follow-up, which was the primary outcome of this study.

RESULTS: Sixty-three patients (72 eyes) were followed for a median of 16 months (range, 3-36 months). Atrophy at baseline was observed in 47% (34/72) of eyes; progression of atrophy occurred in 62% (45/72) of eyes at the last visit. The number of anti-vascular endothelial growth factor injections received was statistically significantly associated with the progression of atrophy at follow-up (odds ratio, 1.35; 95% confidence interval, 1.05-1.73; $P = 0.02$).

CONCLUSION: Atrophy was frequently observed in patients with age-related macular degeneration and choroidal neovascular membranes undergoing anti-vascular endothelial growth factor therapy.

PMID: 22846802 [PubMed - as supplied by publisher]

Nihon Ganka Gakkai Zasshi. 2012 Jul;116(7):643-9.

[Retinal and choroidal thickness changes following intravitreal ranibizumab injection for exudative age-related macular degeneration]. [Article in Japanese]

Ogasawara M, Maruko I, Sugano Y, Ojima A, Sekiryu T, Iida T.

Department of Ophthalmology, Fukushima Medical University School of Medicine, Japan
mogasawara2@yahoo.co.jp

PURPOSE: To evaluate the retinal and choroidal thickness changes following intravitreal ranibizumab injection (IVR) for exudative age-related macular degeneration (AMD).

METHODS: Twenty-eight eyes of 28 patients (average age 72.2) with newly diagnosed AMD (typical AMD 24 and PCV 4) were retrospectively examined during a 1-year follow-up. All cases first received 3 consecutive monthly injections and thereafter pro re nata (PRN) retreatment. Central retinal thickness and subfoveal choroidal thickness were measured before and 1, 3, 6 and 12 months after initial treatment using optical coherence tomography.

RESULTS: The average number of injections was 5.2 times. Mean central retinal thickness significantly decreased from 456 microm at baseline to 337 microm 1 month after IVR and 280 microm 1-year after initial IVR (respectively, $p < 0.01$). Mean subfoveal choroidal thickness was 225 microm (typical AMD was 227 microm at baseline) at baseline, 225 microm 6 months after initial IVR and 220 microm 1-year after initial IVR. There was no significant difference compared to baseline ($p = 0.78$ and 0.45).

CONCLUSIONS: Although central retinal thickness of AMD decreased even 1-year after initial IVR, subfoveal choroidal thickness remained at 6 months and 1-year after initial IVR. Subfoveal choroidal thickness of AMD is less affected by IVR in the long term.

PMID: 22844783 [PubMed - in process]

BMJ. 2012 Jul 30;345:e5161. doi: 10.1136/bmj.e5161.

Primary care trusts reverse advice to ophthalmologists to use cheaper drug for wet age related macular degeneration.

Hawkes N.

PMID: 22846417 [PubMed - in process]

Other treatment & diagnosis

Retina. 2012 Jul 30. [Epub ahead of print]

TYPE 1 (SUB-RETINAL PIGMENT EPITHELIAL) NEOVASCULARIZATION IN CENTRAL SEROUS CHORIORETINOPATHY MASQUERADING AS NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

Fung AT, Yannuzzi LA, Bailey Freund K.

*The LuEsther T. Mertz Retinal Research Center of Manhattan Eye, Ear & Throat Hospital and Vitreous-Retina-Macula Consultants of New York, New York †Department of Ophthalmology, New York University, New York, New York ‡Edward S. Harkness Eye Institute, Columbia University College of Physicians and Surgeons, New York, New York.

PURPOSE: The purpose of this study was to describe clinical and multimodal imaging features of patients with Type 1 neovascularization who lack findings of age-related macular degeneration but instead have features consistent with long-standing central serous chorioretinopathy (CSC).

METHODS: Nonconsecutive, retrospective, observational case series. Two groups of patients were identified and analyzed. Group 1 included patients presenting with Type 1 neovascularization who at the time of diagnosis were found to have findings more consistent with long-standing CSC than age-related macular degeneration. Group 2 included patients with a known history of CSC who developed Type 1 neovascularization over their course of follow-up. Clinical histories and multimodal imaging findings (color and red-free photography, fundus autofluorescence imaging, fluorescein angiography, indocyanine green angiography, spectral domain optical coherence tomography, and enhanced depth imaging optical coherence tomography) were analyzed.

RESULTS: Twenty-seven eyes of 22 patients were identified. Thirteen patients presented with Type 1 neovascularization thought to be secondary to CSC (Group 1), and 9 patients with CSC were observed to develop Type 1 neovascularization over their course of follow-up (Group 2). Eight patients (36%) had polypoidal neovascular structures within their Type 1 neovascular lesions, of which 4 (18% of all patients) had bilateral Type 1 neovascularization. The mean age of patients was 61 years (range, 48-76 years), and the median age was 58.5 years. Thirteen patients (59%) were men. For those patients in Group 2, the mean duration between diagnosis of CSC and detection of Type 1 neovascularization was 139 months (range, 7-365 months). The mean subfoveal choroidal thickness was 354 μm (range, 186-666 μm).

CONCLUSION: Some patients presenting with Type 1 neovascularization may have clinical and multimodal imaging findings more consistent with long-standing CSC than with age-related macular degeneration. These patients are more likely to be younger, men, have thicker choroids, and have a higher prevalence of polypoidal neovascularopathy than those patients with Type 1 neovascularization secondary to age-related macular degeneration. Proper identification of these patients may have implications for their natural course and management.

PMID: 22850219 [PubMed - as supplied by publisher]

Hum Mol Genet. 2012 Jul 26. [Epub ahead of print]

Non-syndromic retinal ciliopathies: translating gene discovery into therapy.

Estrada-Cuzcano A, Roepman R, Cremers FP, den Hollander AI, Mans DA.

Department of Human Genetics.

Abstract

Homozygosity mapping and exome sequencing have accelerated the discovery of gene mutations and modifier alleles implicated in inherited retinal degeneration in humans. To date, 158 genes have been found to be mutated in individuals with retinal dystrophies. Approximately one-third of the gene defects underlying retinal degeneration affect the structure and/or function of the "connecting cilium" in photoreceptors. This structure corresponds to the transition zone of a prototypic cilium, a region with increasing relevance for ciliary homeostasis. The connecting cilium connects the inner and outer segment of the photoreceptor, mediating bi-directional transport of phototransducing proteins required for vision. In fact, the outer segment, connecting cilium and associated basal body forms a highly specialized sensory cilium, fully dedicated to photoreception and subsequent signal transduction to the brain. At least 21 genes that encode ciliary proteins are implicated in non-syndromic retinal dystrophies like cone dystrophy (CD), cone-rod dystrophy (CRD), Leber congenital amaurosis (LCA), macular degeneration (MD) or retinitis pigmentosa (RP). The generation and characterization of vertebrate retinal ciliopathy animal models have revealed insights into the molecular disease mechanism which are indispensable for the development and evaluation of therapeutic strategies. Gene augmentation therapy has proven to be safe and successful in restoring long-term sight in mice, dogs and humans suffering from LCA or RP. Here, we present a comprehensive overview of the genes, mutations and modifier alleles involved in non-syndromic retinal ciliopathies, review the progress in dissecting the associated retinal disease mechanisms, and evaluate gene augmentation approaches to antagonize retinal degeneration in these ciliopathies.

PMID: 22843501 [PubMed - as supplied by publisher]

Am J Pathol. 2012 Jul 26. [Epub ahead of print]

Prospective Treatment of Age-Related Diseases by Slowing Down Aging.

Blagosklonny MV.

Department of Cell Stress Biology, Roswell Park Cancer Institute, Buffalo, New York.

Abstract

Atherosclerosis, hypertension, obesity, diabetic complications, cancer, benign prostate hyperplasia, Alzheimer and Parkinson diseases, age-related macular degeneration, osteoarthritis, osteoporosis, and seborrheic keratosis are strongly associated with aging, implying a common underlying process. Each disease is treated separately and, in most cases, symptomatically. Suppression of aging itself should delay or treat all age-related diseases, thus increasing healthy life span and maximal longevity. But, is it possible to slow down aging? Recent evidence indicates that the target of rapamycin signaling pathway is involved in cellular senescence and organismal aging. Preclinical and clinical studies demonstrated the therapeutic effects of rapamycin in diverse age-related diseases. One simple reason why a single drug is indicated for so many age-related diseases is that it inhibits the aging process.

PMID: 22841821 [PubMed - as supplied by publisher]

BMC Ophthalmol. 2012 Jul 30;12(1):31. [Epub ahead of print]

Profile of patients presenting at a low vision clinic in a developing country.

Olusanya B, Onoja G, Ibraheem W, Bekibele C.

BACKGROUND: Low vision is an important public health problem; however, very few low vision clinics are available to address the needs of low vision patients in most developing countries. The purpose of this study was to describe the characteristics of patients attending the low vision clinic of a Nigerian tertiary hospital.

METHODS: This was a prospective cross sectional study of all new patients seen at the low vision clinic

over a 36 month period. Patients were administered with a structured questionnaire, and were examined and tested with low vision devices by the attending low vision specialist. Information on the demographic and clinical characteristics of the patients was recorded.

RESULTS: A total of 193 new patients seen during the period were studied. The mean age was 41.4 years, and their ages ranged between 6 and 90 years with a male to female ratio of 1.9:1. Majority (58%) were aged below 50 years, 23.3% were children ([less than or equal to]15 years), while 21.8% were elderly patients ([greater than or equal to]65 years). The commonest cause of low vision was retinitis pigmentosa (16.6%); 14.5% had age related macular degeneration (ARMD); 9.8% had albinism; while only 1% had diabetic retinopathy. ARMD(45.2%) was the commonest cause in the elderly patients, while albinism (24.4%) and optic atrophy (24.4%) were the commonest in children.

CONCLUSION: The demographic and clinical characteristics of low vision patients seen in this clinic are similar to that of patients in other developing countries, but different from those in developed countries. Elderly patients and females may be under-utilising low vision services. There is a need for further research into the determinants of low vision service utilisation in developing countries. This would further aid the planning and delivery of services to low vision patients in these countries.

PMID: 22846399 [PubMed - as supplied by publisher]

Nihon Ganka Gakkai Zasshi. 2012 Jul;116(7):635-42.

[Detection for retinal pigment epithelial lesions in fellow eye of age-related macular degeneration by retro-mode].[Article in Japanese]

Takeda M, Sato Y, Ogino T, Imaizumi H, Okushiba U, Kinoshita T, Miyamoto H.

Souen Muneyasu Eye Clinic, Sapporo, Japan. takedamnj@ybb.ne.jp

PURPOSE: Using the Retro-mode (RM), to detect drusen and other minute lesions of the retinal pigment epithelium (RPE) invisible in current imaging methods in the fellow eye of Japanese patients with exudative age-related macular degeneration(AMD).

DESIGN: A retrospective cross-sectional study.

PATIENTS AND METHODS: The fellow eyes of nineteen Japanese patients with unilateral exudative AMD were examined using RM imaging (F-10 fundus camera, Nidek), in contrast with fluorescein angiography, indocyanine green angiography, and optic coherence tomography (3D OCT-1000, Topcon Co). We were able to identify the type of drusen and minute granular lesions (MGLs) in the RPE.

RESULTS: In all patients, RM imaging gave easier to identify images of all types of drusen than other current imaging methods. Moreover, MGLs of the RPE either adjacent to drusen or without drusen, invisible in other current methods, were detected by RM imaging.

CONCLUSIONS: The RM provides clearer imaging of all kind of drusen, and MGLs of the RPE invisible with current methods. These MGLs are possible precursors of drusen.

PMID: 22844782 [PubMed - in process]

Pathogenesis

Am J Pathol. 2012 Jul 26. [Epub ahead of print]

Adrenomedullin Inhibits Choroidal Neovascularization via CCL2 in the Retinal Pigment Epithelium.

Yuda K, Takahashi H, Inoue T, Ueta T, Iriyama A, Kadonosono K, Tamaki Y, Aburatani H, Nagai R, Yanagi Y.

Department of Ophthalmology, University of Tokyo School of Medicine, Tokyo, Japan.

Abstract

The molecular mechanism that leads to age-related macular degeneration (AMD) is poorly understood. Gene expression profiling identified adrenomedullin (ADM) as a possible molecular target for the treatment of AMD and expression of ADM was upregulated in eyes with laser-induced choroidal neovascularization (CNV). In vivo experiments strongly indicated that ADM inhibits laser-induced CNV. In vitro tube formation assay demonstrated that neither ADM nor conditioned medium from the retinal pigment epithelial (RPE) cells, D407 cells, treated with ADM affected the capillary-formation of human umbilical vein endothelial cells. In contrast, in vitro macrophage migration assay clearly demonstrated that the conditioned medium of D407 inhibited macrophage migration. Furthermore, the expression of C-C motif chemokine 2 (CCL2) was significantly inhibited in D407 cells after ADM treatment. In vivo experiments using a laser-induced CNV model in ADM(+/-) mice demonstrated that CCL2 expression was upregulated in ADM(+/-) mice with concomitant increase in macrophage migration in the subretinal space. Additionally, the effect of ADM was abrogated in CCL2 knockout mice. These results suggest that administration of ADM inhibits macrophage migration in the subretinal space and leads to the suppression of laser-induced CNV in an animal model. The inhibition of macrophage migration occurred through the CCL2 from RPE. This study provides a novel potential therapeutic target for AMD which does not substantially disrupt VEGF-A signaling mediated vasculogenesis.

PMID: 22841816 [PubMed - as supplied by publisher]

Neuron. 2012 Jul 26;75(2):271-82.

Photochemical restoration of visual responses in blind mice.

Polosukhina A, Litt J, Tochitsky I, Nemargut J, Sychev Y, De Kouchkovsky I, Huang T, Borges K, Trauner D, Van Gelder RN, Kramer RH.

Vision Science Graduate Group, University of California, Berkeley, Berkeley, CA 94720, USA.

Abstract

Retinitis pigmentosa (RP) and age-related macular degeneration (AMD) are degenerative blinding diseases caused by the death of rods and cones, leaving the remainder of the visual system intact but largely unable to respond to light. Here, we show that AAQ, a synthetic small molecule photoswitch, can restore light sensitivity to the retina and behavioral responses in vivo in mouse models of RP, without exogenous gene delivery. Brief application of AAQ bestows prolonged light sensitivity on multiple types of retinal neurons, resulting in synaptically amplified responses and center-surround antagonism in arrays of retinal ganglion cells (RGCs). Intraocular injection of AAQ restores the pupillary light reflex and locomotory light avoidance behavior in mice lacking retinal photoreceptors, indicating reconstitution of light signaling to brain circuits. AAQ and related photoswitch molecules present a potential drug strategy for restoring retinal function in degenerative blinding diseases.

PMID: 22841312 [PubMed - in process] PMCID: PMC3408583 [Available on 2013/7/26]

Nihon Ganka Gakkai Zasshi. 2012 Jul;116(7):609-11.

[Study of pathophysiology of age-related macular degeneration].[Article in Japanese]

Yuzawa M.

PMID: 22844779 [PubMed - in process]

Genetics

Pharmacogenomics. 2012 Jul;13(9):1037-53.

Pharmacogenetics of antiangiogenic and antineovascular therapies of age-related macular degeneration.

Agosta E, Lazzeri S, Orlandi P, Figus M, Fioravanti A, Di Desidero T, Sartini MS, Nardi M, Danesi R, Bocci G.

Division of Pharmacology, Department of Internal Medicine, University of Pisa, Via Roma, 55-56125, Pisa, Italy.

Abstract

Age-related macular degeneration (AMD), the most common age-related disease causing irreversible visual loss in industrialized countries, is a complex and multifactorial illness. Researchers have found components of the complement alternative pathway inside drusen and Bruch's membrane of AMD patients, underlying a possible important role of complement factor H in the pathogenesis of AMD. The neovascular (wet) AMD is the most destructive form and it is characterized by invasion of new blood vessels into subretinal spaces with subsequent exudation and bleeding, resulting in scarring of the macular region and loss of the central vision. The hallmark of the neovascular form is the choroidal neovascularization, where VEGF-A has an important role in the pathogenesis of the disease. SNPs of these genes have recently been investigated as potential pharmacogenetic markers of the antiangiogenic and antineovascular therapy of AMD, which includes verteporfin photodynamic therapy and anti-VEGF-A drugs, such as pegaptanib, bevacizumab and ranibizumab. The CFH rs1061170 CT and TT genotypes have been associated with an improvement of visual acuity in bevacizumab or ranibizumab treated patients, whereas patients harboring VEGF-A rs699946 G allele responded better to bevacizumab-based therapy if compared with patients carrying the A allele. In conclusion, the discovery of pharmacogenetic markers for the personalization of the antiangiogenic and/or antineovascular therapy could be, in the future, a key issue in ophthalmology to obtain a personalization of the therapy and to avoid unnecessary costs and adverse drug reactions.

PMID: 22838951 [PubMed - in process]

Diet

Ophthalmology. 2012 Jul 26. [Epub ahead of print]

The Age-Related Eye Disease Study 2 (AREDS2): Study Design and Baseline Characteristics (AREDS2 Report Number 1).

The AREDS2 Research Group; Writing Committee, Chew EY, Clemons T, Sangiovanni JP, Danis R, Domalpally A, McBee W, Sperduto R, Ferris FL; AREDS2 Research Group(□).

Division of Epidemiology and Clinical Applications, National Eye Institute/National Institutes of Health, Bethesda, Maryland.

PURPOSE:

The Age-Related Eye Disease Study (AREDS) demonstrated beneficial effects of oral supplementation with antioxidant vitamins and minerals on the development of advanced age-related macular degeneration (AMD) in persons with at least intermediate AMD (bilateral large drusen with or without pigment changes). Observational data suggest that other oral nutrient supplements might further reduce the risk of progression to advanced AMD. The primary purpose of the Age-Related Eye Disease Study 2 (AREDS2) is to evaluate the efficacy and safety of lutein plus zeaxanthin (L+Z) and/or ω-3 long-chain polyunsaturated fatty acid

(LCPUFA) supplementation in reducing the risk of developing advanced AMD. The study also assesses the reduction in zinc and the omission of β -carotene from original AREDS formulation.

DESIGN: Multicenter, phase III, randomized, controlled clinical trial.

PARTICIPANTS: Persons aged 50 to 85 with bilateral intermediate AMD or advanced AMD in 1 eye.

METHODS: All participants were randomly assigned to placebo (n = 1012), L+Z (10 mg/2 mg; n = 1044), ω -3 LCPUFAs (eicosapentaenoic acid + docosahexaenoic acid [650 mg/350 mg]; n = 1069), or the combination of L+Z and ω -3 LCPUFAs (n = 1078). All participants were offered a secondary randomization to 1 of 4 variations of the original AREDS formulation keeping vitamins C (500 mg) and E (400 IU) and copper (2 mg) unchanged while varying zinc and β -carotene as follows: Zinc remains at the original level (80 mg), lower only zinc to 25 mg, omit β -carotene only, or lower zinc to 25 mg and omit β -carotene.

MAIN OUTCOME MEASURES: Progression to advanced AMD determined by centralized grading of annual fundus photographs.

RESULTS: We enrolled 4203 participants at 82 clinical centers located in the United States. Population characteristics at baseline were as follows: Mean age, 74 years; 57% female; 97% white; 7% current smokers; 19% with prior cardiovascular disease; and 44% and 50% taking statin-class cholesterol-lowering drugs and aspirin, respectively. Ocular characteristics include 59% with bilateral large drusen, 32% with advanced AMD in 1 eye and mean visual acuity of 20/32 in eyes without advanced AMD.

CONCLUSIONS: This report presents the AREDS2 study design and the participants' baseline demographic and ocular characteristics.

PMID: 22840421 [PubMed - as supplied by publisher]

Ophthalmology. 2012 Aug 1. [Epub ahead of print]

Effect of Lutein and Zeaxanthin on Macular Pigment and Visual Function in Patients with Early Age-Related Macular Degeneration.

Ma L, Yan SF, Huang YM, Lu XR, Qian F, Pang HL, Xu XR, Zou ZY, Dong PC, Xiao X, Wang X, Sun TT, Dou HL, Lin XM.

Department of Nutrition and Food Hygiene, School of Public Health, Peking University, Beijing, China.

PURPOSE: To determine whether supplementation with lutein and zeaxanthin improves macular pigment and visual function in patients with early age-related macular degeneration (AMD).

DESIGN: Randomized, double-masked, placebo-controlled trial.

PARTICIPANTS: Participants with probable AMD who were 50 to 79 years of age were screened for study eligibility from the local communities. One hundred eight subjects with early AMD were recruited.

INTERVENTION: Early AMD patients were assigned randomly to receive 10 mg/day lutein (n = 27), 20 mg/day lutein (n = 27), 10 mg/day lutein plus 10 mg/day zeaxanthin (n = 27); or placebo (n = 27) for 48 weeks. Macular pigment optical density (MPOD) and visual function variables were assessed at baseline, 24 weeks, and 48 weeks.

MAIN OUTCOME MEASURES: The primary outcome was MPOD. Secondary outcomes were visual function variables including best-corrected visual acuity (BCVA), contrast sensitivity (CS), photorecovery time, and Amsler grid testing results.

RESULTS: Macular pigment optical density increased significantly by a mean $\pm$ standard error of 0.076 ± 0.022 density unit in the 20-mg lutein group and 0.058 ± 0.027 density unit in the lutein and

zeaxanthin group during 48 weeks. There was a significant dose-response effect for lutein supplementation, and the changes in MPOD from baseline to 48 weeks were correlated negatively with baseline MPOD in all active treatment groups ($r = -0.56$; $P < 0.001$). At 48 weeks, a trend toward improvement was seen in BCVA, and there was a significant between-group difference in CS at 3 and 6 cycles/degree between the 20-mg lutein group and the placebo group. The increase in MPOD related positively to the reduction in the logarithm of the minimum angle of resolution BCVA ($r = -0.31$; $P < 0.01$) and the increases in CS at 4 spatial frequencies (r ranging from 0.26 to 0.38; all $P < 0.05$).

CONCLUSIONS: Among patients with early AMD, supplementation with lutein and zeaxanthin improved macular pigment, which played a causative role in boosting visual function and might prevent the progression of AMD. Future studies are required to evaluate the effect of these carotenoids on the incidence of late AMD.

PMID: 22858124 [PubMed - as supplied by publisher]

Evid Based Complement Alternat Med. 2012;2012:429124. Epub 2012 Jul 18.

A Longitudinal Follow-Up Study of Saffron Supplementation in Early Age-Related Macular Degeneration: Sustained Benefits to Central Retinal Function.

Piccardi M, Marangoni D, Minnella AM, Savastano MC, Valentini P, Ambrosio L, Capoluongo E, Maccarone R, Bisti S, Falsini B.

Dipartimento di Scienze Otorinolaringoiatriche e Oftalmologiche, Università Cattolica del Sacro Cuore, 00168 Roma, Italy.

Objectives: In a previous randomized clinical trial (Falsini et al. (2010)), it was shown that short-term Saffron supplementation improves retinal flicker sensitivity in early age-related macular degeneration (AMD). The aim of this study was to evaluate whether the observed functional benefits from Saffron supplementation may extend over a longer follow-up duration.

Design: Longitudinal, interventional open-label study. **Setting:** Outpatient ophthalmology setting. **Participants.** Twenty-nine early AMD patients (age range: 55-85 years) with a baseline visual acuity > 0.3 . **Intervention.** Saffron oral supplementation (20 mg/day) over an average period of treatment of 14 (± 2) months.

Measurements: Clinical examination and focal-electroretinogram-(fERG-) derived macular (18°) flicker sensitivity estimate (Falsini et al. (2010)) every three months over a followup of 14 (± 2) months. Retinal sensitivity, the reciprocal value of the estimated fERG amplitude threshold, was the main outcome measure.

Results: After three months of supplementation, mean fERG sensitivity improved by 0.3 log units compared to baseline values ($P < 0.01$), and mean visual acuity improved by two Snellen lines compared to baseline values (0.75 to 0.9, $P < 0.01$). These changes remained stable over the follow-up period. **Conclusion.** These results indicate that in early AMD Saffron supplementation induces macular function improvements from baseline that are extended over a long-term followup.

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Am J Epidemiol. 2012 Jul 29. [Epub ahead of print]

20/20--Alcohol and Age-related Macular Degeneration: The Melbourne Collaborative Cohort Study.

Adams MK, Chong EW, Williamson E, Aung KZ, Makeyeva GA, Giles GG, English DR, Hopper J, Guymer RH, Baird PN, Robman LD, Simpson JA.

Abstract

Little evidence exists regarding associations between age-related macular degeneration (AMD) and moderate alcohol consumption, patterns of consumption, or different types of alcoholic beverage. The authors examined associations between AMD prevalence and alcohol intake using 20,963 participants from the Melbourne Collaborative Cohort Study aged 40-69 years at baseline (1990-1994). Participants' alcohol consumption was determined from a structured interview at baseline. At follow-up from 2003 to 2007, digital macula photographs of both eyes were taken and evaluated for early and late AMD signs. Drinking more than 20 g of alcohol per day was associated with an approximate 20% increase in the odds of early AMD (odds ratio = 1.21, 95% confidence interval: 1.06, 1.38; $P = 0.004$) when compared with those who reported no alcohol intake at baseline, having adjusted for sex, age, smoking, country of birth, education, physical activity, and energy from food. This positive association was apparent for wine, beer, and spirits. The estimates were similar for both sexes. The odds ratio for those drinking more than 20 g of alcohol per day for late AMD was 1.44 (95% confidence interval: 0.85, 2.45; $P = 0.17$). These results show a modest association between alcohol consumption and increased AMD risk.

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