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MD Research News

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Drug treatment

Eye (Lond). 2014 May 16. doi: 10.1038/eye.2014.101. [Epub ahead of print]

Visual and anatomical outcomes following intravitreal aflibercept in eyes with recalcitrant neovascular age-related macular degeneration: 12-month results.

Grewal DS, Gill MK, Sarezky D, Lyon AT, Mirza RG.

Purpose: To describe the efficacy of intravitreal aflibercept on 12-month visual and anatomical outcomes in patients with neovascular age-related macular degeneration (AMD) recalcitrant to prior monthly intravitreal bevacizumab or ranibizumab.

Methods: Non-comparative case series of 21 eyes of 21 AMD patients with evidence of persistent exudation (intraretinal fluid/cysts, or subretinal fluid (SRF), or both) on spectral domain OCT despite ≥6 prior intravitreal 0.5 mg ranibizumab or 1.25 mg bevacizumab (mean 29.8±17.1 injections) over 31.6±17.4 months who were transitioned to aflibercept.

Results: At baseline, best-corrected visual acuity (BCVA) was 0.42±0.28 logarithm of minimum-angle of resolution (logMAR), central foveal thickness (CFT) was 329.38±102.67 μm and macular volume (MV) was 7.71±1.32 mm3. After 12 months of aflibercept (mean 10.2±1.2 injections), BCVA was 0.40±0.28 logMAR (P=0.5), CFT decreased to 292.71±91.35 μm (P=0.038) and MV improved to 7.33±1.27 mm3 (P=0.003). In a subset of 15 eyes with a persistent fibrovascular or serous pigment epithelial detachment (PED), mean baseline PED greatest basal diameter (GBD) was 2350.9±1067.6 μm and mean maximal height (MH) was 288.7±175.9 μm. At 12 months, GBD improved to 1896.3±782.3 μm (P=0.028), while MH decreased to 248.27±146.2 μm (P=0.002).

Conclusion: In patients with recalcitrant AMD, aflibercept led to anatomic improvement at 12 months, reduction in proportion of eyes with SRF and reduction in PED, while preserving visual acuity.

PMID: 24833178 [PubMed - as supplied by publisher]

J Ocul Pharmacol Ther. 2014 May 12. [Epub ahead of print]

Long-Term Visual Outcome and Its Predictive Factors Following Treatment of Acute Submacular Hemorrhage with Intravitreous Injection of Tissue Plasminogen Factor and Gas.

Sobolewska B, Utebey E, Bartz-Schmidt KU, Tatar O.

Abstract Purpose: To investigate the long-term functional outcome and its predictive factors of treatment of acute submacular hemorrhage secondary to age-related macular degeneration with intravitreal application

of recombinant tissue plasminogen activator (rt-PA) and gas.

Methods: Twenty-six patients were enrolled in the retrospective case series. A complete history and ocular examination, including fluorescein angiography, were performed. The best-corrected visual acuity was measured with a Snellen chart. Patients were followed up for 12 to 131 months (mean: 49 months). All patients underwent intravitreal injection of rt-PA (50 µg) and expansile gas. Primary outcome measures were best postoperative and final visual acuity and degree of blood displacement.

Results: The size of the subretinal hemorrhage ranged from 0.5 to 28 disc diameters, and the degree of blood displacement was defined as complete (≥1 disc area from the center of the fovea), partial, or no displacement. Twenty-one (81%) patients showed partial or complete displacement of hemorrhage. Due to lack of displacement of hemorrhage in 5 patients (19%), submacular surgery was performed. In 13 of 21 (62%; P=0.0001) patients with displacement of hemorrhage, the best postoperative visual acuity improved ≥2 lines. The final visual acuity improved ≥2 lines in 42.9% (9 of 21), was stable in 23.8% (5 of 21), and worse ≥2 lines in 33.3% (7 of 21) of patients. The short duration of hemorrhage (≤4 days) and complete displacement of blood, independent of the hemorrhage size, were significantly associated with better postoperative visual acuity (P=0.0001, P=0.0001, respectively).

Conclusion: Intravitreal injection of rt-PA and gas seem to be more effective when applied within the first 4 days of acute submacular hemorrhage. Preoperative visual acuity as well as displacement of hemorrhage might be useful to predict final visual acuity.

PMID: 24821566 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2014 May 6. pii: S0002-9394(14)00233-5. doi: 10.1016/j.ajo.2014.04.029. [Epub ahead of print]

Predictors of Sustained Intraocular Pressure Elevation in Eyes Receiving Intravitreal Anti-Vascular Endothelial Growth Factor Therapy.

Yannuzzi NA, Patel SN, Bhavsar KV, Sugiguchi F, Freund KB.

PURPOSE: To determine the intravitreal anti-vascular endothelial growth factor (VEGF) injection techniques and preferences within the retinal community and to identify potential factors associated with the development of sustained intraocular pressure (IOP) elevation in patients treated with intravitreal anti-VEGF therapy for neovascular age-related macular degeneration (AMD).

DESIGN: Cross-sectional, physician survey.

METHODS: Five-hundred-thirty retina specialists spanning both private and academic practices were surveyed regarding current anti-VEGF intravitreal injection protocols including the anti-VEGF drug of choice, needle gauge, injection volume, injection technique, and self-reported prevalence of sustained IOP elevation. Multivariate logistic regressions were performed to assess the potential influence of these factors on long-term IOP.

RESULTS: Two-hundred-ninety-two (55%) specialists reported believing that intravitreal anti-VEGF therapy may cause sustained IOP elevation. Of these responses, the most common reported prevalence was 1-2% (48%) followed by 3-5% (34%). There was no relationship between the frequency of sustained IOP elevation and anti-VEGF drug of choice. Physicians who injected greater than 0.05cc in less than one second were 5.56 times more likely to observe a high frequency of sustained IOP elevation (p=0.006, 95% C.I. 1.64-18.89).

CONCLUSIONS: Based on physician survey data, serial anti-VEGF injections using higher injection volumes with a rapid injection technique may potentially lead to sustained IOP elevation. The underlying mechanism for this complication may be injury to the trabecular meshwork resulting from rapid elevations in IOP. Further investigation of the relationship between injection techniques and sustained IOP elevation in

the form of retrospective or prospective clinical studies is warranted.

PMID: 24814167 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Br J Ophthalmol. 2014 May 12. doi: 10.1136/bjophthalmol-2013-304761. [Epub ahead of print]

Proton beam irradiation for non-AMD CNV: 2-year results of a randomised clinical trial.

Chen L, Kim IK, Lane AM, Gauthier D, Munzenrider JE, Gragoudas ES, Miller JW.

AIMS: To evaluate safety and visual outcomes after proton beam irradiation (PBI) therapy for subfoveal choroidal neovascularisation (CNV) secondary to causes other than age-related macular degeneration (AMD).

METHODS: This study is a prospective, unmasked and randomised clinical trial using two dosage regimens, conducted in the Massachusetts Eye and Ear Infirmary. The study included 46 patients with CNV secondary to non-AMD and best-corrected visual acuity of 20/320 or better. Patients were randomly assigned to receive 16 or 24 cobalt gray equivalents (CGE) of PBI in two equal fractions. Complete ophthalmological examinations, fundus photography and fluorescein angiography were performed at baseline and 6, 12, 18 and 24 months after treatment.

RESULTS: At 1 year after treatment, 82% and 72% lost fewer than 1.5 lines of vision in the 16 CGE and in 24 CGE groups, respectively. At 2 years after therapy, 77% in the lower dose group and 64% in the higher dose group lost fewer than 1.5 lines of vision. Mild radiation complications such as radiation vasculopathy developed in 17.6% of patients.

CONCLUSIONS: PBI is a safe and efficacious treatment for subfoveal CNV not due to AMD. The data with respect to visual outcomes and radiation complications trend in favour of the 16 CGE group, although differences do not reach statistical significance. PBI may be considered as an alternative to current therapies.

PMID: 24820046 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2014 May 15. pii: bjophthalmol-2014-305032. doi: 10.1136/bjophthalmol-2014-305032. [Epub ahead of print]

Gaze and pupil changes during navigation in age-related macular degeneration.

Aspinall PA, Borooah S, Al Alouch C, Roe J, Laude A, Gupta R, Gupta M, Montarzino A, Dhillon B.

BACKGROUND: The central visual field is particularly affected in age-related macular degeneration (AMD), and this can impinge on a variety of functional tasks, including navigation, which can affect activities of daily living. It has been difficult to assess navigational function under standardised conditions. The aim of this study is to examine gaze function and pupil diameter during navigation in patients with AMD.

METHODS: This study was designed as an observational case-control investigation. 34 patients with AMD and 23 controls were recruited. We simulated a walking journey using video projection and monitored patients using automated eye tracking. Visual acuity, fixation count, fixation duration and pupil diameter were recorded while subjective measurements included recorded voice comments.

RESULTS: The pupil diameters were significantly greater in the AMD group compared with the control group in both easy and difficult segments of navigation (p=0.002). Fixation counts were significantly higher in the AMD group during difficult segments of navigation (p=0.001). The differences in both pupil diameter

and fixation count correlated with subject visual acuity.

CONCLUSIONS: Fixation count is a marker of difficult navigational environments in patients with AMD. The combination of video projection and eye tracking to assess visual navigation function is a useful clinical tool and an adjunct to current investigation tools in AMD intervention studies providing objective clinical measures under standardised settings.

PMID: 24831715 [PubMed - as supplied by publisher]

Retina. 2014 May 14. [Epub ahead of print]

MORPHOLOGIC FEATURES OF FOCAL CHOROIDAL EXCAVATION ON SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY WITH SIMULTANEOUS ANGIOGRAPHY.

Shinojima A, Kawamura A, Mori R, Yuzawa M.

PURPOSE: To reveal clinically relevant morphologic findings in patients with focal choroidal excavation (FCE) using enhanced depth imaging optical coherence tomography.

METHODS: Thirty-one FCE lesions in 29 eyes of 26 patients (21 men, 23 eyes; 5 women, 6 eyes) were studies. In all 26 patients, color fundus photographs were obtained, and fluorescein angiography and indocyanine green angiography with simultaneous enhanced depth imaging optical coherence tomography were performed. Twenty-five eyes also underwent angiographic video recording.

RESULTS: Focal choroidal excavation was detected in eyes with typical age-related macular degeneration, central serous chorioretinopathy, polypoidal choroidal vasculopathy, and idiopathic choroidal neovascularization, whereas in 8 eyes, FCE was considered to be idiopathic. Morphologically, FCE lesions were classified into 3 types: cone-shaped, bowl-shaped, and mixed. The cone-shaped type was detected in 17 lesions, bowl-shaped in 8, and mixed in 6, on optical coherence tomography findings. All bowl-shaped and mixed types had retinal pigment epithelial irregularities within the FCE lesion. The cone-shaped type was not observed in eyes with typical age-related macular degeneration.

CONCLUSIONS: Morphologically, FCE lesions were classified into cone-shaped, bowl-shaped, and mixed types, based on optical coherence tomography findings. Focal choroidal excavation formation may be associated in part with chorioretinal diseases such as age-related macular degeneration and central serous chorioretinopathy, whereas some eyes are considered to have idiopathic FCE.

PMID: 24830823 [PubMed - as supplied by publisher]

J Am Soc Mass Spectrom. 2014 May 13. [Epub ahead of print]

High Resolution MALDI Imaging Mass Spectrometry of Retinal Tissue Lipids.

Anderson DM, Ablonczy Z, Koutalos Y, Spraggins J, Crouch RK, Caprioli RM, Schey KL.

Abstract: Matrix assisted laser desorption ionization imaging mass spectrometry (MALDI IMS) has the ability to provide an enormous amount of information on the abundances and spatial distributions of molecules within biological tissues. The rapid progress in the development of this technology significantly improves our ability to analyze smaller and smaller areas and features within tissues. The mammalian eye has evolved over millions of years to become an essential asset for survival, providing important sensory input of an organism's surroundings. The highly complex sensory retina of the eye is comprised of numerous cell types organized into specific layers with varying dimensions, the thinnest of which is the 10 μm retinal pigment epithelium (RPE). This single cell layer and the photoreceptor layer contain the complex biochemical machinery required to convert photons of light into electrical signals that are transported to the brain by axons of retinal ganglion cells. Diseases of the retina, including age-related macular degeneration

(AMD), retinitis pigmentosa, and diabetic retinopathy, occur when the functions of these cells are interrupted by molecular processes that are not fully understood. In this report, we demonstrate the use of high spatial resolution MALDI IMS and FT-ICR tandem mass spectrometry in the Abca4 -/- knockout mouse model of Stargardt disease, a juvenile onset form of macular degeneration. The spatial distributions and identity of lipid and retinoid metabolites are shown to be unique to specific retinal cell layers.

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Curr Eye Res. 2014 May 15:1-18. [Epub ahead of print]

Translating Ocular Biomechanics into Clinical Practice: Current State and Future Prospects.

Girard MJ1, Dupps WJ, Baskaran M, Scarcelli G, Yun SH, Quigley HA, Sigal IA, Strouthidis NG.

Abstract: Biomechanics is the study of the relationship between forces and function in living organisms and is thought to play a critical role in a significant number of ophthalmic disorders. This is not surprising, as the eye is a pressure vessel that requires a delicate balance of forces to maintain its homeostasis. Over the past few decades, basic science research in ophthalmology mostly confirmed that ocular biomechanics could explain in part the mechanisms involved in almost all major ophthalmic disorders such as optic nerve head neuropathies, angle closure, ametropia, presbyopia, cataract, corneal pathologies, retinal detachment and macular degeneration. Translational biomechanics in ophthalmology, however, is still in its infancy. It is believed that its use could make significant advances in diagnosis and treatment. Several translational biomechanics strategies are already emerging, such as corneal stiffening for the treatment of keratoconus, and more are likely to follow. This review aims to cultivate the idea that biomechanics plays a major role in ophthalmology and that the clinical translation, lead by collaborative teams of clinicians and biomedical engineers, will benefit our patients. Specifically, recent advances and future prospects in corneal, iris, trabecular meshwork, crystalline lens, scleral and lamina cribrosa biomechanics are discussed.

PMID: 24832392 [PubMed - as supplied by publisher]

Pathogenesis

PLoS One. 2014 May 14;9(5):e96895. doi: 10.1371/journal.pone.0096895. eCollection 2014.

Proteomics of vitreous humor of patients with exudative age-related macular degeneration.

Koss MJ, Hoffmann J, Nguyen N, Pfister M, Mischak H, Mullen W, Husi H, Rejdak R, Koch F, Jankowski J, Krueger K, Bertelmann T, Klein J, Schanstra JP, Siwy J.

BACKGROUND: There is absence of specific biomarkers and an incomplete understanding of the pathophysiology of exudative age-related macular degeneration (AMD).

METHODS AND FINDINGS: Eighty-eight vitreous samples (73 from patients with treatment naïve AMD and 15 control samples from patients with idiopathic floaters) were analyzed with capillary electrophoresis coupled to mass spectrometry in this retrospective case series to define potential candidate protein markers of AMD. Nineteen proteins were found to be upregulated in vitreous of AMD patients. Most of the proteins were plasma derived and involved in biological (ion) transport, acute phase inflammatory reaction, and blood coagulation. A number of proteins have not been previously associated to AMD including alpha-1-antitrypsin, fibrinogen alpha chain and prostaglandin H2-D isomerase. Alpha-1-antitrypsin was validated in vitreous of an independent set of AMD patients using Western blot analysis. Further systems biology analysis of the data indicated that the observed proteomic changes may reflect upregulation of immune response and complement activity.

CONCLUSIONS: Proteome analysis of vitreous samples from patients with AMD, which underwent an

intravitreal combination therapy including a core vitrectomy, steroids and bevacizumab, revealed apparent AMD-specific proteomic changes. The identified AMD-associated proteins provide some insight into the pathophysiological changes associated with AMD.

PMID: 24828575 [PubMed - in process]

Mol Neurobiol. 2014 May 15. [Epub ahead of print]

Interconnection Between Brain and Retinal Neurodegenerations.

Jindal V.

Abstract: The eye is a special sensory organ, which is basically an extension of the brain. Both are derived from neural tube and consist of neurons. Therefore, diseases of both the brain and eye should have some similarity. Neurodegenerative disorders like Alzheimer's disease (AD) is the major cause of dementia in the world. Amyloid deposition in the cerebral cortex and hippocampal region is the basic pathology in AD. But along with it, there are various changes that take place in the eye, i.e., abnormal pupillary reaction, decreased vision, decreased contrast sensitivity, visual field changes, loss of retinal ganglionic cells and retinal fiber layer, peripapillary atrophy, increased cup-disk ratio, retinal thinning, tortuosity of blood vessels, and deposition of Aβ-like substance in the retina. And these changes are present in the early part of the disease when only mild cognitive impairment is there. As the brain is covered by a hard bony skull which makes it difficult to directly visualize the changes occurring in the brain at molecular levels, finer details of disease progression are not available with us. But the eye is the window of the brain; with advanced modern techniques, we can directly visualize the changes in the retina at a very fine level. Therefore, by depicting neurodegenerative changes in the eye, we can diagnose and manage AD at very early stages. Along with it, retinal neurodegenerations like glaucoma and age-related macular degeneration (ARMD) are the major cause of loss of vision, and still, there are no effective treatment modalities for these blinding conditions. So if we can understand its pathogenesis and progression by correlating with brain neurodegenerations, we can come up with a better therapy for glaucoma and ARMD.

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Invest Ophthalmol Vis Sci. 2014 May 15. pii: IOVS-14-14051. doi: 10.1167/iovs.14-14051. [Epub ahead of print]

RETINAL MICROGLIA ARE ACTIVATED BY SYSTEMIC FUNGAL INFECTION.

Maneu V, Noailles A, Megías J, Gómez-Vicente V, Carpena N, Gil ML, Gozalbo D, Cuenca N.

Purpose: To determine whether systemic fungal infection could cause activation of retinal microglia and therefore could be potentially harmful for patients with retinal degenerative diseases.

Methods: Activation of retinal microglia was measured in a model of sublethal invasive candidiasis in C57BL/6J mice by (i) confocal immunofluorescence and (ii) flow cytometry analysis, using anti-CD11b, anti-Iba1, anti-MHCII and anti-CD45 antibodies.

Results: Systemic fungal infection causes activation of retinal microglia, with phenotypic changes in morphology, surface markers expression, and microglial re-location in retinal layers.

Conclusions: As an excessive or prolonged microglial activation may lead to chronic inflammation with severe pathological side effects, causing or worsening the course of retinal dystrophies, a systemic infection may represent a risk factor to be considered in patients with ocular neurodegenerative diseases, such as diabetic retinopathy, glaucoma, age-related macular degeneration or retinitis pigmentosa.

PMID: 24833742 [PubMed - as supplied by publisher]

Epidemiology

Ophthalmology. 2014 May 6. pii: S0161-6420(14)00246-2. doi: 10.1016/j.ophtha.2014.03.022. [Epub ahead of print]

Age-Related Macular Degeneration: Prevalence and Risk Factors from Korean National Health and Nutrition Examination Survey, 2008 through 2011.

Park SJ, Lee JH, Woo SJ, Ahn J, Shin JP, Song SJ, Kang SW, Park KH; Epidemiologic Survey Committee of the Korean Ophthalmologic Society.

OBJECTIVE: To investigate the prevalence and risk factors of age-related macular degeneration (AMD) in the Korean population.

DESIGN: A cross-sectional study using a complex, stratified, multistage, probability-cluster survey, which can produce nationally representative estimates.

PARTICIPANTS: Using the database of Korean National Health and Nutrition Examination Survey from 2008 through 2011, 14 352 participants 40 years of age or older with gradable fundus photographs were included.

METHODS: Age-related macular degeneration was determined by fundus photograph. Prevalences of AMDs were estimated. Risk factor analyses were conducted using logistic regression analyses (LRAs).

MAIN OUTCOME MEASURES: Prevalence and risk factors of AMD.

RESULTS: The prevalence of AMD was 6.62% (95% confidence interval [CI], 6.15%-7.09%) in the Korean population: 6.02% (95% CI, 5.56%-6.48%) were early AMD and 0.60% (95% CI, 0.45%-0.75%) were late AMD. The prevalence of early AMD in women (6.73%; 95% CI, 6.11%-7.35%) was higher than that in men (5.25%; 95% CI, 4.61%-5.89%; P<0.001), and the prevalence of late AMD in women (0.37%; 95% CI, 0.22%-0.52%) was lower than that in men (0.85%; 95% CI, 0.59%-1.12%; P<0.001). However, in multiple LRAs both early and late AMD had no association with gender, house income, residence, sun exposure, or systemic comorbidities, including hypertension, diabetes mellitus, and cardiovascular diseases. Early AMD had positive associations with older age groups (P<0.001), lower education (P = 0.027), occupation (P<0.001), anemia (P = 0.027), hepatitis B surface antigen carrier status (P<0.001), not being overweight (body mass index [BMI], P = 0.032; waist circumference, P = 0.041, in separate analyses), and higher serum high-density lipoprotein (HDL) level (P = 0.046), but not with smoking status. Late AMD had positive associations with age groups (P<0.001), current smokers (P = 0.022), and lower BMI (P = 0.037).

CONCLUSIONS: The results suggest that there are 1.21 million individuals with early AMD and 121 000 individuals with late AMD in Korea. Nonoverweight status and higher HDL levels, generally assumed as positive health indicators, as well as anemia and hepatitis B infection had harmful associations with AMD in our study, implying a possible different pathophysiologic process of AMD in Asians compared with that of white persons.

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Genetics

Am J Clin Nutr. 2014 May 14. pii: ajcn.071563. [Epub ahead of print]

Macular xanthophylls, lipoprotein-related genes, and age-related macular degeneration.

Koo E, Neuringer M, SanGiovanni JP.

Abstract: Plant-based macular xanthophylls (MXs; lutein and zeaxanthin) and the lutein metabolite meso-

zeaxanthin are the major constituents of macular pigment, a compound concentrated in retinal areas that are responsible for fine-feature visual sensation. There is an unmet need to examine the genetics of factors influencing regulatory mechanisms and metabolic fates of these 3 MXs because they are linked to processes implicated in the pathogenesis of age-related macular degeneration (AMD). In this work we provide an overview of evidence supporting a molecular basis for AMD-MX associations as they may relate to DNA sequence variation in AMD- and lipoprotein-related genes. We recognize a number of emerging research opportunities, barriers, knowledge gaps, and tools offering promise for meaningful investigation and inference in the field. Overviews on AMD- and high-density lipoprotein (HDL)-related genes encoding receptors, transporters, and enzymes affecting or affected by MXs are followed with information on localization of products from these genes to retinal cell types manifesting AMD-related pathophysiology. Evidence on the relation of each gene or gene product with retinal MX response to nutrient intake is discussed. This information is followed by a review of results from mechanistic studies testing gene-disease relations. We then present findings on relations of AMD with DNA sequence variants in MX-associated genes. Our conclusion is that AMD-associated DNA variants that influence the actions and metabolic fates of HDL system constituents should be examined further for concomitant influence on MX absorption, retinal tissue responses to MX intake, and the capacity to modify MX-associated factors and processes implicated in AMD pathogenesis.

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Invest Ophthalmol Vis Sci. 2014 May 15. pii: IOVS-13-13099. doi: 10.1167/iovs.13-13099. [Epub ahead of print]

Mutant ELOVL4 that causes autosomal dominant Stargardt-3 macular dystrophy is misrouted to rod outer segment disks.

Agbaga MP, Tam BM, Wong JS, Yang LL, Anderson RE, Moritz OL.

Purpose: Autosomal dominant Stargardt macular dystrophy caused by mutations in the Elongation of Very Long Chain fatty acids (ELOVL4) gene results in macular degeneration, leading to early childhood blindness. Transgenic mice and pigs expressing mutant ELOVL4 develop progressive photoreceptor degeneration. The mechanism by which these mutations cause macular degeneration remains unclear, but have been hypothesized to involve the loss of an ER-retention dilysine motif located in the extreme C-terminus. Dominant negative mechanisms and reduction in retinal polyunsaturated fatty acids have also been suggested. To understand the molecular mechanisms involved in disease progression in vivo, we addressed the hypothesis that the disease-linked C-terminal truncation mutant of ELOVL4 exerts a dominant negative effect on wild type (WT) ELOVL4, altering its subcellular localization and function, which subsequently induces retinal degeneration and loss of vision.

Methods: We generated transgenic X. laevis that over-express HA-tagged murine ELOVL4 variants in rod photoreceptors.

Results: Tagged or untagged WT ELOVL4 localized primarily to inner segments. However, the mutant protein lacking the dilysine motif was mislocalized to post-Golgi compartments and outer segment disks. Co-expression of mutant and WT ELOVL4 in rods did not result in mislocalization of the WT protein to outer segments or in the formation of aggregates. Full-length HA-tagged ELOVL4 lacking the dilysine motif (K308R/K310R) necessary for targeting the WT ELOVL4 protein to the endoplasmic reticulum was similarly mislocalized to outer segments.

Conclusions: We propose that outer segment mislocalization of the disease-linked 5 base-pair deletion mutant ELOVL4 protein alters photoreceptor structure and function, which subsequently results in retinal degeneration, and suggest three possible mechanisms by which mutant ELOVL4 may induce retinal degeneration in STGD3.

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Diet & lifestyle

Eye (Lond). 2014 May 16. doi: 10.1038/eye.2014.100. [Epub ahead of print]

Smoking and choroidal thickness in patients over 65 with early-atrophic age-related macular degeneration and normals.

Sigler EJ, Randolph JC, Calzada JI, Charles S.

Objective: To compare macular choroidal thickness between cigarette smokers, those with a history of smoking, and nonsmokers in patients over 65 years of age with early-atrophic age-related macular degeneration (AMD) and normals.

Methods: Prospective, consecutive, observational case series. Enhanced depth imaging spectral domain optical coherence tomography 12-line radial scans were performed and choroidal thickness manually quantified at 84 points in the central 3 mm of the macula. Data of normals, soft drusen alone, and soft drusen with additional features of early AMD were compared. A multivariate analysis of variance (MANOVA) model, controlling for age, was constructed to evaluate the effect of smoking history and AMD features on choroidal thickness.

Results: A history of smoking was significantly associated with a thinner choroid across all patients via logistic regression (P=0.004; O.R.=12.4). Mean macular choroidal thickness was thinner for smokers (148±63 μm) than for nonsmokers (181±65 μm) among all diagnosis categories (P=0.003). Subgroup analysis of patients with AMD features revealed a similar decreased choroidal thickness in smokers (121±41 μm) compared with nonsmokers (146±46 μm, P=0.006). Bivariate analysis revealed an association between increased pack-years of smoking and a thin choroid across all patients (P<0.001) and among patients with features of early AMD (P<0.001). Both the presence of features of macular degeneration (P<0.001) and a history of smoking (P=0.024) were associated with decreased choroidal thickness in a MANOVA model.

Conclusion: Chronic cigarette smoke exposure may be associated with decreased choroidal thickness. There may be an anatomic sequelae to chronic tobacco smoke exposure that underlies previously reported AMD risk.

PMID: 24833184 [PubMed - as supplied by publisher]

Ophthalmologica. 2014;231(4):185-90. doi: 10.1159/000357528.

Evidence-based nutritional advice for patients affected by age-related macular degeneration.

Andreatta W, El-Sherbiny S.

Abstract: This paper presents the evidence available in the literature on the role of nutrients in preventing the occurrence of age-related macular degeneration (AMD) and its progression to more advanced stages. In our analysis we considered publications on vitamins B, C, E and D, carotenoids (i.e. lutein, zeaxanthin and β-carotene), Ω-3 polyunsaturated fatty acids and zinc published between 2003 and 2013. While the evidence supporting supplementation and higher dietary intake of nutrients for AMD prevention is weak to moderate, large and robust randomised controlled trials showed that the AREDS formula leads to a 25% reduction in progression to advanced AMD in individuals belonging to AREDS categories 3 and 4. After reviewing the current literature, which includes the AREDS2 study, we suggest an 'evidence-based formula'.

PMID: 24821294 [PubMed - in process]