Macular Disease Foundation AUSTRALIA
Our focus is your vision

MD Research News

Issue 157

Monday 18 November, 2013

Drug treatment

PLoS One. 2013 Oct 25;8(10):e78538. doi: 10.1371/journal.pone.0078538.

Efficacy and safety of intravitreal therapy in macular edema due to branch and central retinal vein occlusion: a systematic review.

Pielen A, Feltgen N, Isserstedt C, Callizo J, Junker B, Schmucker C.

University Eye Hospital, Albert Ludwig University, Freiburg, Germany ; University Eye Hospital, Medical School of Hannover, Hannover, Germany.

BACKGROUND: Intravitreal agents have replaced observation in macular edema in central (CRVO) and grid laser photocoagulation in branch retinal vein occlusion (BRVO). We conducted a systematic review to evaluate efficacy and safety outcomes of intravitreal therapies for macular edema in CRVO and BRVO.

METHODS: And Findings: MEDLINE, Embase, and the Cochrane Library were systematically searched for RCTs with no limitations of language and year of publication. 11 RCTs investigating anti-VEGF agents (ranibizumab, bevacizumab, aflibercept) and steroids (triamcinolone, dexamethasone implant) with a minimum follow-up of 1 year were evaluated.

EFFICACY CRVO: Greatest gain in visual acuity after 12 months was observed both under aflibercept 2 mg: +16.2 letters (8.5 injections), and under bevacizumab 1.25 mg: +16.1 letters (8 injections). Ranibizumab 0.5 mg improved vision by +13.9 letters (8.8 injections). Triamcinolone 1 mg and 4 mg stabilized visual acuity at a lower injection frequency (-1.2 letters, 2 injections).

BRVO: Ranibizumab 0.5 mg resulted in a visual acuity gain of +18.3 letters (8.4 injections). The effect of dexamethasone implant was transient after 1.9 implants in both indications.

SAFETY: Serious ocular adverse events were rare, e.g., endophthalmitis occurred in 0.0-0.9%. Major differences were found in an indirect comparison between steroids and anti-VEGF agents for cataract progression (19.8-35.0% vs. 0.9-7.0%) and in required treatment of increased intraocular pressure (7.0-41.0% vs. none). No major differences were identified in systemic adverse events.

CONCLUSIONS: Anti-VEGF agents result in a promising gain of visual acuity, but require a high injection frequency. Dexamethasone implant might be an alternative, but comparison is impaired as the effect is temporary and it has not yet been tested in PRN regimen. The ocular risk profile seems to be favorable for anti-VEGF agents in comparison to steroids. Because comparative data from head-to-head trials are missing currently, clinicians and patients should carefully weigh the benefit-harm ratio.

PMID: 24205253 [PubMed - in process] PMCID: PMC3808377

Ophthalmologica. 2013 Nov 2. [Epub ahead of print]

Cardiac Issues of Noncardiac Drugs: The Rising Story of Avastin in Age-Related Macular Degeneration.

Cruess AF, Giacomantonio N.

Capital Health, Dalhousie University, Halifax, N.S., Canada.

Abstract: Emerging safety data, accompanied with recent demographic trends, point to the need for an in-depth review and consideration of potential consequences that might arise from continuing use of bevacizumab (Avastin®) to treat elderly patients presenting with wet age-related macular degeneration (AMD). Although it is expected that lower doses of Avastin used for intravitreal administration and an intact blood-retina barrier would reduce the systemic exposure of the drug, both animal and human studies suggest that this may not be the case. In addition, emerging real-world and clinical trial data continue to point toward compromises in both cardio- and cerebrovascular safety with Avastin. Thus, clinicians are urged to adopt the highest possible standard of care in the treatment of an already fragile AMD population. Furthermore, postmarketing surveillance and pharmacovigilance with intravitreal anti-VEGF inhibitors should remain a priority.

PMID: 24217407 [PubMed - as supplied by publisher]

Curr Eye Res. 2013 Nov 11. [Epub ahead of print]

Intravitreal Injection of Ranibizumab for Treatment of Age-Related Macular Degeneration: Effects on Serum VEGF Concentration.

Gu X, Yu X, Dai H.

Department of Ophthalmology, Beijing Hospital of the Ministry of Health , Beijing , China.

Abstract Aims: To evaluate potential adverse ranibizumab-related systemic events through analysis of variations in serum levels of vascular endothelial growth factor (VEGF) in neovascular age-related macular degeneration (AMD) patients before and after a single intravitreal injection of ranibizumab.

Methods: Thirty-nine patients with neovascular AMD and 39 healthy control subjects were enrolled in the study. Patients received a single intravitreal injection of ranibizumab (0.5 mg) in one eye. Venous blood was collected and placed in coagulation-promoting tubes 1 day before and on post-injection days 1, 3, 7 and 30. Serum concentrations of VEGF were measured by ELISA at each time point.

Results: VEGF concentrations were 323.64 pg/ml in AMD patients and 392.94 pg/ml in control subjects before injection ($p > 0.05$). VEGF significantly decreased to 304.65 pg/ml 1 day later ($p < 0.05$) in AMD patients, then increased to 310.77 ($p > 0.05$), 317.89 ($p > 0.05$) and 311.79 pg/ml ($p > 0.05$) on post-injection days 3, 7 and 30, respectively.

Conclusion: No significant changes in serum levels of VEGF were found from 3 to 30 days following a single intravitreal ranibizumab injection. Although certain influences existed 24-h post-injection, effect(s) of a single intravitreal ranibizumab injection on the homeostasis of the cardiovascular system during such a brief period is unknown.

PMID: 24215127 [PubMed - as supplied by publisher]

Expert Opin Drug Deliv. 2013 Nov 13. [Epub ahead of print]

Drug delivery techniques for treating age-related macular degeneration.

Schwartz SG, Scott IU, Flynn HW Jr, Stewart MW.

University of Miami Miller School of Medicine, Bascom Palmer Eye Institute , 311 9th Street North, Naples, 34102 , USA.

Introduction: Currently, the standard therapy for neovascular age-related macular degeneration involves the use of anti-vascular endothelial growth factor (VEGF) drugs, which are delivered by repeated office-based intravitreal injections. This treatment is generally very effective in stabilizing or improving vision, although repeated injections create a burden for patients, family members and physicians. In addition, the cumulative risks of endophthalmitis and other complications increase with the number of injections.

Areas covered: In the clinic, much attention is focused on the relative efficacies of the three major anti-VEGF medications (bevacizumab, ranibizumab and aflibercept) as well as the most popular re-injection regimens (monthly, as-needed and treat-and-extend). In theory, intravitreal anti-VEGF drug delivery with sustained-release devices would offer similar visual results with fewer required re-injections. Various approaches have been studied, including noninvasive techniques, intraocular implants and colloidal carriers, such as liposomes, microparticles and nanoparticles.

Expert opinion: Despite its theoretical appeal, sustained-release drug delivery will not replace current techniques unless it offers one or more advantages in efficacy, safety, convenience or cost. Currently, many patients maintain stable vision with intravitreal injections at intervals of 2 months or longer, so sustained-release techniques will have to lengthen these intervals substantially to become widely accepted. As we continue to collect data from clinical trials, the role of sustained-release techniques will become better defined.

PMID: 24219407 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2013 Nov 8. doi: 10.1111/aos.12300. [Epub ahead of print]

Electrophysiological toxicity testing of VEGF Trap-Eye in an isolated perfused vertebrate retina organ culture model.

Januschowski K, Schnichels S, Hagemann U, Koch V, Hofmann J, Spitzer MS, Bartz-Schmidt KU, Szurman P, Lüke M, Aisenbrey S.

Center for Ophthalmology, University Eye Hospital, Eberhard-Karls University of Tübingen, Tübingen, Germany.

PURPOSE: Age-related macular degeneration (AMD) is the leading cause of visual impairment in Western nations. Since the discovery of the importance of vascular endothelial growth factor (VEGF) in the pathogenesis of neovascular AMD, anti-VEGF agents including pegaptanib, ranibizumab and bevacizumab provide a treatment option to improve vision in affected persons. VEGF Trap-Eye (Aflibercept) is a new agent available for the treatment of exudative AMD. The molecule is a receptor decoy with a longer half-life and a higher affinity to VEGF compared with ranibizumab or bevacizumab. The presented study has been designed to evaluate the short-term toxic effects of VEGF Trap-Eye on retinal function during and after direct exposure to the drug.

METHODS: Isolated bovine retinas were perfused with an oxygen-saturated nutrient solution, and the electroretinogram (ERG) was recorded using silver/silver chloride electrodes. A total of 0.5 mg or 2 mg VEGF Trap-Eye was added to the nutrient solution and retinas were exposed for 45 min, followed by a washout period of 100 min. The percentage of a- and b-wave reduction at the end of the washout was compared with the baseline values. Additionally, retinal whole mount cultures were exposed for 24 hr to VEGF Trap-Eye, and the amount of apoptotic cells were determined using the terminal deoxynucleotidyl transferase-mediated uridine 5'-triphosphate-biotin nick end labelling (TUNEL) assay.

RESULTS: During simulation of intraocular application, no significant reduction in the a-wave amplitude for

0.5 mg (2.70%, p = 0.37) and 2 mg (3.84%, p = 0.37) VEGF Trap-Eye and b-wave amplitude for 0.5 mg (19.68%, p = 0.17) and 2 mg (24.1%, p = 0.06) VEGF Trap-Eye was observed at the end of the washout. However, there were significant changes in a-wave and b-wave amplitudes directly after exposure to 0.5 mg VEGF Trap-Eye (18.4%, p = 0.004 and 43.1%, p = 0.006, respectively).

CONCLUSIONS: The presented data suggest that intraocular application of up to 2 mg VEGF Trap-Eye does not induce irreversible toxic retinal damage. However, short-term results showed a negative effect directly after the application for 0.5 mg and 2 mg VEGF Trap-Eye.

PMID: 24206925 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2013 Nov;91 Thesis7:1-22. doi: 10.1111/aos.12272.

Implementation studies of ranibizumab for neovascular age-related macular degeneration.

Bloch SB.

Department of Ophthalmology, Glostrup Hospital, Glostrup, Denmark; Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark.

PMID: 24206851 [PubMed - in process]

Indian J Ophthalmol. 2013 Nov 11. [Epub ahead of print]

A case of subacute cutaneous lupus erythematosus as a result of ranibizumab (Lucentis) treatment.

Andric M, Dixit S, Robaei D, Watchorn R, Verma N.

Department of Ophthalmology, Royal Hobart Hospital, Tasmania, Australia.

Abstract: Cutaneous lupus erythematosus is a previously undiagnosed side-effect of ranibizumab. Here, we present a case of an 82-year-old female Caucasian patient with wet age-related macular degeneration. Following a single intraocular injection of Lucentis (ranibizumab), she developed a subacute cutaneous lupus erythematosus which, with treatment, took nearly 12 months to resolve. This shows that cutaneous lupus erythematosus is a potential side-effect of many medications, including ranibizumab, as in our case and, in an aging population where polypharmacy is a growing reality, clinicians should be aware of how to diagnose and best manage such cases.

PMID: 24212210 [PubMed - as supplied by publisher]

Saudi J Ophthalmol. 2013 Apr;27(2):79-82. doi: 10.1016/j.sjopt.2013.01.002. Epub 2013 Jan 31.

Ranibizumab for idiopathic epiretinal membranes: A retrospective case series.

Abouammoh MA, Belliveau MJ, Almeida DR, Gale JS, Sharma S.

Department of Ophthalmology, College of Medicine, King Saud University, Riyadh, Saudi Arabia ; Department of Ophthalmology, Hotel Dieu Hospital, Queen's University, Kingston, Ontario, Canada.

PURPOSE: To study the effect of intravitreal ranibizumab on idiopathic epiretinal membranes (ERMs).

METHODS: A retrospective cohort study on a consecutive series of ranibizumab intravitreal injections for epiretinal membranes was performed. Four cases were identified by reviewing a claims database linked to electronic medical records. All patients received a total of three 0.05 mg/0.05 ml ranibizumab intravitreal injections at a monthly interval. The primary outcome measure was the final best-corrected visual acuity

(BCVA) at the end of the injection series, and the final central macular thickness (CMT).

RESULTS: All four patients completed 3 months follow-up after the last ranibizumab injection. The mean baseline CMT was 509 microns (SD = 111). A trend was noticed for reduction in CMT (Δ = 41 microns) P = 0.08. Three patients improved by one line in their BCVA. The remaining patient maintained the same BCVA. No complications were noted.

CONCLUSION: In this study, intravitreal injection of ranibizumab marginally reduced retinal thickness in four patients with minimal improvement in visual acuity. No safety concerns were noticed. Further basic science and clinical studies may be warranted to assess the role of vascular endothelial growth factor and the effect of ranibizumab on idiopathic epiretinal membranes.

PMID: 24227966 [PubMed]

Mediators Inflamm. 2013;2013:476525. Epub 2013 Oct 21.

Topical Nonsteroidal Anti-Inflammatory Drugs for Macular Edema.

Russo A, Costagliola C, Delcassi L, Parmeggiani F, Romano MR, Dell'omo R, Semeraro F.

Eye Clinic, Department of Neurological and Vision Sciences, University of Brescia, Piazzale Spedale Civili 1, 25123 Brescia, Italy.

Abstract: Nonsteroidal anti-inflammatory drugs (NSAIDs) are nowadays widely used in ophthalmology to reduce eye inflammation, pain, and cystoid macular edema associated with cataract surgery. Recently, new topical NSAIDs have been approved for topical ophthalmic use, allowing for greater drug penetration into the vitreous. Hence, new therapeutic effects can be achieved, such as reduction of exudation secondary to age-related macular degeneration or diabetic maculopathy. We provide an updated review on the clinical use of NSAIDs for retinal diseases, with a focus on the potential future applications.

PMID: 24227908 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2013 Nov 13. doi: 10.1136/bjophthalmol-2013-303954. [Epub ahead of print]

Vascular endothelial growth factor suppression times in patients with diabetic macular oedema treated with ranibizumab.

Muether PS, Droege KM, Fauser S.

Department of Ophthalmology, University of Cologne, Cologne, Germany.

BACKGROUND: To measure vascular endothelial growth factor (VEGF) levels in aqueous humour from patients with diabetic macular oedema (DME) treated with ranibizumab and to determine how long VEGF was suppressed.

METHODS: In this nonrandomised, prospective clinical study, 17 eyes of 17 patients were included in the study. A total of 110 aqueous humour samples were taken before an intravitreal ranibizumab injection in patients with DME. VEGF-A was measured by Luminex multiplex bead analysis (Luminex Inc, USA).

RESULTS: VEGF was completely suppressed in all patients after ranibizumab injections for a mean of 33.7 days (SD±5.1, range 27-42, median 34). VEGF suppression times were individually stable during the observation time of up to 16 months. There was no statistically significant difference of VEGF levels at baseline and before the beginning of a new injection series (123.6 pg/mL vs 125.1 pg/mL; p=1.0, Wilcoxon).

CONCLUSIONS: Monthly ranibizumab injections lead to a complete VEGF suppression in patients with DME. The long-term stability and the range of suppression times among individuals suggest that some

patients could benefit from individual injection intervals.

PMID: 24227804 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2013 Nov 13. doi: 10.1136/bjophthalmol-2013-303117. [Epub ahead of print]

Pazopanib eye drops: a randomised trial in neovascular age-related macular degeneration.

Danis R, McLaughlin MM, Tolentino M, Staurenghi G, Ye L, Xu CF, Kim RY, Johnson MW; for the Pazopanib Eye Drops Study Group.

Collaborators (19)

Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, USA.

AIMS: To evaluate pazopanib eye drops in patients with subfoveal choroidal neovascularisation secondary to age-related macular degeneration.

METHODS: 70 patients with minimally classic or occult subfoveal choroidal neovascularisation were randomly assigned to 5 mg/mL TID, 2 mg/mL TID, and 5 mg/mL QD pazopanib eye drops for 28 days in a multicentre, double-masked trial with an optional safety extension for up to 5 additional months. The primary outcomes were central retinal thickness (CRT) and best-corrected visual acuity (BCVA) at Day 29.

RESULTS: No significant decrease from baseline in CRT was observed overall; however, an exploratory analysis showed improvement in CRT (mean decrease of 89 μm) in patients with the CFH TT genotype who received 5 mg/mL TID (p=0.01, n=5). Mean increases in BCVA were observed in the 5 mg/mL TID overall (4.32 letters (p=0.002, n=26)) and in those that with CFH Y402H TT (6.96 letters (p=0.02, n=5)) and CT (4.09 letters (p=0.05, n=9)) genotypes. No safety signals that precluded continued investigation were detected.

CONCLUSIONS: 5 mg/mL pazopanib eye drops resulted in mean improvement in BCVA at Day 29 and improvements in vision. However, improvement in macular oedema for age-related macular degeneration was found only in the subset of subjects with the CFH Y402H TT genotype, warranting further investigation.

PMID: 24227801 [PubMed - as supplied by publisher]

BMJ Case Rep. 2013 Nov 13;2013. pii: bcr2013010203. doi: 10.1136/bcr-2013-010203.

Durable recovery of the macular architecture and functionality of a diagnosed age-related macular degeneration 1 year after a single intravitreal injection of dobesilate.

Cuevas P, Outeiriño LA, Azanza C, Giménez-Gallego G.

Departamento de Investigación, IRYCIS, Hospital Universitario Ramón y Cajal, Madrid, Spain.

Abstract: Among the age-related diseases that affect vision, age-related macular degeneration is the most frequent cause of blindness in patients older than 60 years. In this communication, we report the full anatomical and functional recovery of a patient diagnosed with wet age-related macular degeneration 1 year after a single intravitreal injection of dobesilate.

PMID: 24225910 [PubMed - in process]

J Fr Ophtalmol. 2013 Oct 24. pii: S0181-5512(13)00292-1. doi: 10.1016/j.jfo.2013.02.008. [Epub ahead of print]

Correlation between aqueous flare and chorioretinal neovascularization in age-related macular degeneration following intravitreal bevacizumab injections.

Errera MH, Girmens JF, Ayello-Scheer S, Nourry H, Warnet JM, Sahel JA, Barale PO.

Department of Ophthalmology IV, Centre hospitalier National des Quinze-Vingts, 28, rue de Charenton, 75012 Paris, France. Electronic address: marie-helene.errera@orange.fr.

PURPOSE: Prospective evaluation of aqueous flare following intravitreal bevacizumab (Avastin, Genentech Inc., San Francisco, CA, USA) injections in eyes with choroidal neovascularization due to age-related macular degeneration.

PATIENTS AND METHODS: Sixteen eyes of eight patients were recruited. Aqueous humor flare was determined by laser flare meter every month after one intravitreal injection of 1.25mg of bevacizumab at baseline followed by a second injection at month3 (day 100±21days). Four patients received an injection at month6 (±10days), and one patient received an injection at month7.

RESULTS: Two months after the first intravitreal bevacizumab injection, flare values decreased from 10±5.57 (mean±standard deviation) to 5.2±1.69photon count/ms (P=0.0207) and from 8.3±3.59 to 5.4±0photon counts/ms, 2months after the second injection (P=0.02).

CONCLUSION: Significantly decreased aqueous humor flare levels were noted after repeated injections of bevacizumab.

PMID: 24209785 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Prog Retin Eye Res. 2013 Nov 6. pii: S1350-9462(13)00069-4. doi: 10.1016/j.preteyeres.2013.10.002. [Epub ahead of print]

Progress on Retinal Image Analysis for Age Related Macular Degeneration.

Kanagasingam Y, Bhuiyan A, Abràmoff MD, Smith RT, Goldschmidt L, Wong TY.

Australian e-Health Research Centre, Commonwealth Scientific and Industrial Research Organization (CSIRO), Underwood Avenue, WA 6014, Australia. Electronic address: http://aehrc.com/

Abstract: Age-related macular degeneration (AMD) is the leading cause of vision loss in those over the age of 50 years in the developed countries. The number is expected to increase by ~1.5 fold over the next ten years due to an increase in ageing population. One of the main measures of AMD severity is the analysis of drusen, pigmentary abnormalities, geographic atrophy (GA) and choroidal neovascularization (CNV) from imaging based on colour fundus photograph, optical coherence tomography (OCT) and other imaging modalities. Each of these imaging modalities has strengths and weaknesses for extracting individual AMD pathology and different imaging techniques are used in combination for capturing and/or quantification of different pathologies. Current dry AMD treatments cannot cure or reverse vision loss. However, the Age-Related Eye Disease Study (AREDS) showed that specific anti-oxidant vitamin supplementation reduces the risk of progression from intermediate stages (defined as the presence of either many medium-sized drusen or one or more large drusen) to late AMD which allows for preventative strategies in properly identified patients. Thus identification of people with early stage AMD is important to design and implement preventative strategies for late AMD, and determine their cost-effectiveness. A mass screening facility with teleophthalmology or telemedicine in combination with computer-aided analysis for large rural-based communities may identify more individuals suitable for early stage AMD prevention. In this review, we

discuss different imaging modalities that are currently being considered or used for screening AMD. In addition, we look into various automated and semi-automated computer-aided grading systems and related retinal image analysis techniques for drusen, geographic atrophy and choroidal neovascularization detection and/or quantification for measurement of AMD severity using these imaging modalities. We also review the existing telemedicine studies which include diagnosis and management of AMD, and how automated disease grading could benefit telemedicine. As there is no treatment for dry AMD and only early intervention can prevent the late AMD, we emphasize mass screening through a telemedicine platform to enable early detection of AMD. We also provide a comparative study between the imaging modalities and identify potential study areas for further improvement and future research direction in automated AMD grading and screening.

PMID: 24211245 [PubMed - as supplied by publisher]

Ophthalmology. 2013 Nov 8. pii: S0161-6420(13)00952-4. doi: 10.1016/j.ophtha.2013.10.027. [Epub ahead of print]

Randomized Trial of a Home Monitoring System for Early Detection of Choroidal Neovascularization Home Monitoring of the Eye (HOME) Study.

The AREDS2-HOME Study Research Group, Chew WC, Clemons TE, Bressler SB, Elman MJ, Danis RP, Domalpally A, Heier JS, Kim JE, Garfinkel R.

Clinical Trials Branch, National Eye Institute/National Institutes of Health, Bethesda, Maryland. Electronic address: echew@nei.nih.gov.

OBJECTIVE: To determine whether home monitoring with the ForeseeHome device (Notal Vision Ltd, Tel Aviv, Israel), using macular visual field testing with hyperacuity techniques and telemonitoring, results in earlier detection of age-related macular degeneration-associated choroidal neovascularization (CNV), reflected in better visual acuity, when compared with standard care. The main predictor of treatment outcome from anti-vascular endothelial growth factor (VEGF) agents is the visual acuity at the time of CNV treatment.

DESIGN: Unmasked, controlled, randomized clinical trial.

PARTICIPANTS: One thousand nine hundred and seventy participants 53 to 90 years of age at high risk of CNV developing were screened. Of these, 1520 participants with a mean age of 72.5 years were enrolled in the Home Monitoring of the Eye study at 44 Age-Related Eye Disease Study 2 clinical centers.

INTERVENTIONS: In the standard care and device arms arm, investigator-specific instructions were provided for self-monitoring vision at home followed by report of new symptoms to the clinic. In the device arm, the device was provided with recommendations for daily testing. The device monitoring center received test results and reported changes to the clinical centers, which contacted participants for examination.

MAIN OUTCOME MEASURES: The main outcome measure was the difference in best-corrected visual acuity scores between baseline and detection of CNV. The event was determined by investigators based on clinical examination, color fundus photography, fluorescein angiography, and optical coherence tomography findings. Masked graders at a central reading center evaluated the images using standardized protocols.

RESULTS: Seven hundred sixty-three participants were randomized to device monitoring and 757 participants were randomized to standard care and were followed up for a mean of 1.4 years between July 2010 and December 2013. At the prespecified interim analysis, 82 participants progressed to CNV, 51 in the device arm and 31 in the standard care arm. The primary analysis achieved statistical significance, with the participants in the device arm demonstrating a smaller decline in visual acuity with fewer letters lost

from baseline to CNV detection (median, -4 letters; interquartile range [IQR], -11.0 to -1.0 letters) compared with standard care (median, -9 letters; IQR, -14.0 to -4.0 letters; P = 0.021), resulting in better visual acuity at CNV detection in the device arm. The Data and Safety Monitoring Committee recommended early study termination for efficacy.

CONCLUSIONS: Persons at high risk for CNV developing benefit from the home monitoring strategy for earlier detection of CNV development, which increases the likelihood of better visual acuity results after intravitreal anti-VEGF therapy.

PMID: 24211172 [PubMed - as supplied by publisher]

BMJ Open. 2013 Nov 7;3(11):e003306. doi: 10.1136/bmjopen-2013-003306.

'I'd like to know what causes it, you know, anything I've done?' Are we meeting the information and support needs of patients with macular degeneration? A qualitative study.

Burton AE, Shaw RL, Gibson JM.

Faculty of Health Sciences, Staffordshire University, Stoke-on-Trent, UK.

OBJECTIVE: To examine patients' experiences of information and support provision for age-related macular degeneration (AMD) in the UK.

STUDY DESIGN: Exploratory qualitative study investigating patient experiences of healthcare consultations and living with AMD over 18 months.

SETTING: Specialist eye clinics at a Birmingham hospital.

PARTICIPANTS: 13 patients diagnosed with AMD.

MAIN OUTCOME MEASURES: Analysis of patients' narratives to identify key themes and issues relating to information and support needs.

RESULTS: Information was accessed from a variety of sources. There was evidence of clear information deficits prior to diagnosis, following diagnosis and ongoing across the course of the condition. Patients were often ill informed and therefore unable to self-advocate and recognise when support was needed, what support was available and how to access support.

CONCLUSIONS: AMD patients have a variety of information needs that are variable across the course of the condition. Further research is needed to determine whether these experiences are typical and identify ways of translating the guidelines into practice. Methods of providing information need to be investigated and improved for this patient group.

PMID: 24202055 [PubMed] PMCID: PMC3822314

Retina. 2013 Nov 11. [Epub ahead of print]

CHOROIDAL THICKNESS IN AGE-RELATED MACULAR DEGENERATION.

Jonas JB, Forster TM, Steinmetz P, Schlichtenbrede FC, Harder BC.

Department of Ophthalmology, Medical Faculty Mannheim, Ruprecht-Karls-University, Heidelberg, Germany.

PURPOSE: To examine choroidal thickness in age-related macular degeneration (AMD).

METHODS: The hospital-based case series study included patients with nonexudative or exudative AMD

as study group, and the control group consisted of subjects with a normal fundus. Choroidal thickness was measured by enhanced depth imaging of spectral domain optical coherence tomography.

RESULTS: The study group (126 patients; 204 eyes) included a nonexudative subgroup (n = 50 eyes) and an exudative subgroup (n = 154 eyes), differentiated into eyes with mostly retinal pigment epithelium detachment (n = 35), mostly retinal edema (n = 36), and a subretinal fibrotic scar (n = 83). For 29 patients with unilateral AMD, contralateral normal eyes were compared with affected eyes. The control group consisted of 189 patients (228 eyes). Comparing choroidal thickness between the affected eyes and contralateral unaffected eyes in patients with unilateral AMD revealed no statistically significant differences (all $P > 0.20$). After adjusting for age and refractive error, subfoveal choroidal thickness was not significantly (all $P > 0.10$) related with AMD neither as a whole nor with the nonexudative or exudative AMD subgroup nor with the single exudative AMD subtypes (except for the subretinal fibrotic scar subgroup; $P = 0.03$). Correspondingly, choroidal thickness at a horizontal distance of 1000 µm from the fovea was not significantly (all $P \geq 0.30$) associated with any subgroup of AMD. In binary regression analysis, the presence of AMD or of its subtypes (except for subretinal fibrotic scar type) was not significantly (all $P \geq 0.20$) associated with subfoveal or parafoveal choroidal thickness after adjustment for age and refractive error. After matching for age, refractive error, and axial length, study group and control group did not differ significantly (all $P \geq 0.25$) in foveal or parafoveal choroidal thickness measurements.

CONCLUSION: After adjusting for age and refractive error, AMD, neither in its nonexudative form nor exudative form, was significantly associated with a marked thinning or thickening of the choroid in the foveal and parafoveal region.

PMID: 24220257 [PubMed - as supplied by publisher]

Ophthalmologica. 2013 Nov 6. [Epub ahead of print]

Correlation of Fundus Fluorescein Angiography and Spectral-Domain Optical Coherence Tomography in Identification of Membrane Subtypes in Neovascular Age-Related Macular Degeneration.

Mathew R, Pefkianaki M, Kopsachilis N, Brar M, Richardson M, Sivaprasad S.

Laser and Retinal Research Unit, Department of Ophthalmology, King's College Hospital, London, UK.

Aims: To assess the sensitivity and specificity of spectral-domain optical coherence tomography (SDOCT) for the determination of choroidal neovascularization (CNV) subtypes in neovascular age-related macular degeneration (AMD) compared to fundus fluorescein angiography (FFA) and also the agreement between the two procedures.

Design: This was a retrospective, observational study.

Methods: We evaluated and compared the CNV subtypes on FFA and OCT in 100 eyes initiated on ranibizumab for neovascular AMD.

Results: SDOCT showed high sensitivity (85.7-98.3%) and specificity (84.2-100%) compared to FFA in the diagnosis of the CNV subtype. The area under the receiver-operating characteristic curve ranged from 0.9 to 0.93 (p value <0.0001) for the different CNV subtypes. Weighted kappa statistics showed a near-perfect agreement of 0.85 between the procedures.

Conclusion: SDOCT is a reliable tool for the diagnosis of CNV subtypes in neovascular AMD obviating the need for an invasive procedure such as FFA.

PMID: 24217293 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2013 Nov 7. pii: iovs.13-12284v1. doi: 10.1167/iovs.13-12284. [Epub ahead of print]

Correlation between subfoveal choroidal thickness and the severity or progression of non-exudative age-related macular degeneration.

Lee JY, Lee DH, Lee JY, Yoon YH.

University of Ulsan, Asan Medical Center, Seoul, Korea, Seoul, 138736, Korea (South), Republic of.

Purpose: To investigate the correlation between subfoveal choroidal thickness (SFChT) and the severity or progression of non-exudative age-related macular degeneration (AMD).

Methods: One hundred and seventy six eyes of 114 patients with non-exudative AMD were included in this study. These eyes were divided into stages I-IV, based on the Age Related Eye Disease Study (AREDS) classification of fundus findings. Using enhanced depth imaging from spectralis domain optical coherence tomography (SD-OCT), the central retinal thickness (CRT), SFChT, and parafoveal choroidal thickness (PFChT) were measured. The area of geographic atrophy (GA) was measured from fundus autofluorescence (FAF) images, and the progression of GA was calculated using RegionFinder software.

Results: The age-adjusted SFChT levels were lower at later stages of non-exudative AMD. These measurements were as follows: 266.68 ± 12.60 (stage I: 28 eyes), 263.34 ± 9.87 (stage II: 48 eyes), 200.55 ± 8.83 (stage III: 71 eyes), and 188.34 ± 13.72 (stage IV: 29 eyes) ($p = 0.0028$). The age-adjusted SFChT was also negatively correlated with the best corrected visual acuity (BCVA) (estimate, -0.001; $P = 0.0006$). Among 16 eyes with GA at baseline, SFChT showed a negative correlation with the baseline area of GA ($r = 0.5521$, $p = 0.0133$). In addition, GA progressed more rapidly during the mean follow-up of 22.19 ± 9.08 months when the SFChT was lower at baseline ($r = 0.5658$, $p= 0.0112$).

Conclusions: SFChT is closely related to the BCVA, the severity of non-exudative AMD as well as the rate of GA progression. SFChT may be a predictor of disease progression in GA cases.

PMID: 24204054 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2013;7:2181-2206. Epub 2013 Nov 8.

Clinical applications of optical coherence tomography in the posterior pole: the 2011 José Manuel Espino Lecture - Part II.

Arevalo JF, Lasave AF, Arias JD, Serrano MA, Arevalo FA.

Retina Division, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, MD, USA ; Vitreoretinal Division, King Khaled Eye Specialist Hospital, Riyadh, Kingdom of Saudi Arabia.

Abstract: Optical coherence tomography (OCT) is a high-resolution, cross-sectional imaging technique that allows detailed assessment of retinal thickness and morphologic evaluation of the retinal layers. This technology has developed quickly over the past two decades. OCT imaging has rapidly been integrated into routine ophthalmic clinical practice and trials. It has complemented fluorescein angiography in many instances, especially in the diagnosis and management of retinal disorders, including diabetic macular edema and age-related macular degeneration. With OCT, the exact localization of pathologic features can be visualized in segmentation maps of the retina, and this has allowed OCT to be used to evaluate specific features that may serve as predictive factors in the prognosis and follow up of these pathologies. Therefore, it has become an important clinical and research tool for the diagnosis, follow up, treatment, and assessment of new treatment modalities for all diseases that affect the posterior pole of the eye.

PMID: 24235811 [PubMed - as supplied by publisher]

Saudi J Ophthalmol. 2013 Jul;27(3):209-13. doi: 10.1016/j.sjopt.2013.06.010.

Morphologic changes of the fovea and visual acuity associated with retinal detachment secondary to circumscribed choroidal hemangioma.

Furuta M, Sekiryu T, Kasai A, Oguchi Y.

Department of Ophthalmology, Fukushima Medical University School of Medicine, Fukushima, Japan.

PURPOSE: To clarify and review the early and late morphologic changes of the macula associating with visual loss in patients with subfoveal fluid secondary to extrafoveal circumscribed choroidal hemangiomas.

METHODS: Previously six non-treated eyes of six patients with subfoveal retinal detachment secondary to extrafoveal circumscribed choroidal hemangioma were included. Visual acuity (VA), duration of visual symptoms, color fundus photography, optical coherence tomography (OCT), fundus autofluorescence, and fluorescein angiography (FA) were evaluated.

RESULTS: The mean patient age was 58 years (range, 25-78). The VA and duration of symptoms in each patient was 1.2 (3 days), 0.6 (1 week), 0.4 (3 months), 0.5 (6 months), 0.02 (12 months), and 0.01 (8 years), respectively. Three patients with symptoms for less than 3 months did not have retinal pigment epithelial (RPE) alterations, retinal edema, or thinning of the retinal structure in the fovea. A patient with symptoms for 3 months had subfoveal deposits underneath the detached neurosensory retina with foveal hyperautofluorescence. Two patients with symptoms exceeding 12 months had highly affected RPE and cystoid macular degeneration.

CONCLUSIONS: The VA was affected in patients with longer visual symptoms, and there are some changes in the retina and RPE in the fovea by FA and OCT. Persistent subretinal fluid secondary to choroidal hemangiomas may result in pathologic changes in the neurosensory retina.

PMID: 24227988 [PubMed]

Biomed Eng Online. 2013 Nov 14;12(1):117. [Epub ahead of print]

Automatic analysis of selected choroidal diseases in OCT images of the eye fundus.

Koprowski R, Teper S, Wróbel Z, Wylegala E.

INTRODUCTION: This paper describes a method for automatic analysis of the choroid in OCT images of the eye fundus in ophthalmology. The problem of vascular lesions occurs e.g. in a large population of patients having diabetes or macular degeneration. Their correct diagnosis and quantitative assessment of the treatment progress are a critical part of the eye fundus diagnosis.Material and method: The study analysed about 1'000 OCT images acquired using SOCT Copernicus (Optopol Tech. SA, Zawiercie, Poland). The proposed algorithm for image analysis enabled to analyse the texture of the choroid portion located beneath the RPE (Retinal Pigment Epithelium) layer. The analysis was performed using the profiled algorithm based on morphological analysis and texture analysis and a classifier in the form of decision trees.

RESULTS: The location of the centres of gravity of individual objects present in the image beneath the RPE layer proved to be important in the evaluation of different types of images. In addition, the value of the standard deviation and the number of objects in a scene were equally important. These features enabled classification of three different forms of the choroid that were related to retinal pathology: diabetic edema (the classification gave accuracy ACC1 = 0.73), ischemia of the inner retinal layers (ACC2 = 0.83) and scarring fibro vascular tissue (ACC3 = 0.69). For the cut decision tree the results were as follows: ACC1 = 0.76, ACC2 = 0.81, ACC3 = 0.68.

CONCLUSIONS: The created decision tree enabled to obtain satisfactory results of the classification of

three types of choroidal imaging. In addition, it was shown that for the assumed characteristics and the developed classifier, the location of B-scan does not significantly affect the results. The image analysis method for texture analysis presented in the paper confirmed its usefulness in choroid imaging. Currently the application is further studied in the Clinical Department of Ophthalmology in the District Railway Hospital in Katowice, Medical University of Silesia, Poland.

PMID: 24224964 [PubMed - as supplied by publisher]

Pathogenesis

Inflamm Res. 2013 Nov 8. [Epub ahead of print]

Inflammaging: should this term be suitable for age related macular degeneration too?

Gallenga CE, Parmeggiani F, Costagliola C, Sebastiani A, Gallenga PE.

Section Ophthalmology, Department of Medical-Surgical Communication and Behaviour, University of Ferrara, Ferrara, Italy.

INTRODUCTION: Inflammaging is a phenomenon triggered by the conjunction of chronic repetitive and subclinical inflammation from external aggressors and internal inflammatory mechanisms due to the progressive degradation of systems such as the mitochondrial function. Age-related macular degeneration is the leading cause of blindness and visual impairment in patients older than 60 years in developed countries.

DISCUSSION: Remarkable correlations have been documented between common or rare immunological/ inflammatory gene polymorphisms and AMD, unequivocally indicating the involvement of inflammation and immune-mediated processes (complement activation) in the pathogenesis of this disease.

CONCLUSION: Altogether these factors also drive this pathologic condition under the general heading of "Inflammaging".

PMID: 24202618 [PubMed - as supplied by publisher]

Exp Eye Res. 2013 Nov 8. pii: S0014-4835(13)00313-8. doi: 10.1016/j.exer.2013.10.024. [Epub ahead of print]

Nrf2 signaling is Impaired in the Aging RPE given an Oxidative Insult.

Sachdeva MM, Cano M, Handa JT.

Wilmer Eye Institute, Johns Hopkins School of Medicine.

Abstract: Age-related macular degeneration (AMD) represents the leading cause of blindness in the elderly, yet no definitive therapy exists for early, dry disease. Several lines of evidence have implicated oxidative stress-induced damage to the retinal pigment epithelium (RPE) in the pathogenesis of AMD, suggesting that the aging RPE may exhibit increased susceptibility to cell damage induced by exogenous stressors. The transcription factor Nrf2 serves as the master regulator of a highly coordinated antioxidant response in virtually all cell types. We compared Nrf2 signaling in the RPE of young (2 months) and old (15 months) mice under unstressed and stressed (sodium iodate) conditions. The aging RPE expressed higher levels of the Nrf2 target genes NQO1, GCLM, and HO1 compared with the RPE of younger mice under unstressed conditions, suggesting an age-related increase in basal oxidative stress. Moreover, the RPE of older mice demonstrated impaired induction of the protective Nrf2 pathway following oxidative stress induced with sodium iodate. The RPE of old mice exposed to sodium iodate also exhibited higher levels of superoxide anion and malondialdehyde than young mice, suggesting inadequate protection against oxidative damage.

Induction of Nrf2 signaling in response to sodium iodate was partially restored in the RPE of aging mice with genetic rescue, using conditional knockdown of the Nrf2 negative regulator Keap1 (Tam-Cre;Keap1loxP) compared to Keap1loxP mice. These data indicate that the aging RPE is vulnerable to oxidative damage due to impaired Nrf2 signaling, and that Nrf2 signaling is a promising target for novel pharmacologic or genetic therapeutic strategies.

PMID: 24216314 [PubMed - as supplied by publisher]

Methods Mol Biol. 2014;1100:225-36. doi: 10.1007/978-1-62703-724-2_18.

Factor h-related proteins.

Józsi M, Meri S.

Junior Research Group Cellular Immunobiology, Leibniz Institute for Natural Product Research and Infection Biology, Jena, Germany.

Abstract: Factor H-related proteins (CFHRs) are plasma glycoproteins related in structure and antigenicity to each other and to the complement inhibitory protein factor H. Such proteins are found in most mammals but their number and domain composition vary. This chapter summarizes our current knowledge on the human factor H-related proteins. In contrast to factor H, they have no strong complement inhibitory activity, although for some of them regulatory or complement modulatory activity has been reported. A common feature of CFHRs is that they bind to the C3b component of complement. Novel links between CFHRs and various diseases (C3 glomerulopathies, atypical hemolytic uremic syndrome and age-related macular degeneration) have been revealed in recent years, but we are still far from understanding their biological function.

PMID: 24218263 [PubMed - in process]

Ann Biomed Eng. 2013 Nov 14. [Epub ahead of print]

Discovery of Retinal Elastin and Its Possible Role in Age-Related Macular Degeneration.

Chen K, Weiland JD.

Department of Biomedical Engineering, University of Southern California - Denney Research Center 140, 1042 Downey Way, Los Angeles, CA, 90089, USA, chen0606@umn.edu.

Abstract: Age-related macular degeneration (AMD) etiology is unknown, but its association to atherosclerotic vascular disease (ASVD) has been observed. Since elastin plays an important role in the atherosclerotic process, to understand ASVD and AMD's relationship we examined retinal elastin existence, elastin amount and vessel properties among normal subjects, mild AMD patients, moderate-to-severe AMD patients, and ASVD patients (n = 20). One eye per donor was assigned to enzyme-linked immunosorbent assay for quantifying the retinal elastin amount. The rest were assigned to mechanical test for examining the retinal vessel properties. Additionally, two normal human and two porcine eyes were acquired in immunohistochemistry for locating the retinal elastin. We found that elastin presented in the human and porcine retinal vessels at the basement membranes. 3.73 ± 0.55% of the normal retinal tissues were elastin. Elastin decrease, tissue-weight increase, and vessel hardening and inelasticity ($p < 0.05$) were observed in the retina of patients with ASVD and only moderate-to-severe (i.e., not mild) AMD. Most moderate-to-severe AMD patients also happened to have ASVD. The results suggest that ASVD is unlikely the cause of AMD, but it is perhaps a factor that aggravates the condition through mechanism associated with retinal vessel abnormality.

PMID: 24232693 [PubMed - as supplied by publisher]

J Clin Invest. 2013 Nov 15. pii: 69076. doi: 10.1172/JCI69076. [Epub ahead of print]

Systems pharmacology identifies drug targets for Stargardt disease-associated retinal degeneration.

Chen Y, Palczewska G, Mustafi D, Golczak M, Dong Z, Sawada O, Maeda T, Maeda A, Palczewski K.

Abstract: A systems pharmacological approach that capitalizes on the characterization of intracellular signaling networks can transform our understanding of human diseases and lead to therapy development. Here, we applied this strategy to identify pharmacological targets for the treatment of Stargardt disease, a severe juvenile form of macular degeneration. Diverse GPCRs have previously been implicated in neuronal cell survival, and crosstalk between GPCR signaling pathways represents an unexplored avenue for pharmacological intervention. We focused on this receptor family for potential therapeutic interventions in macular disease. Complete transcriptomes of mouse and human samples were analyzed to assess the expression of GPCRs in the retina. Focusing on adrenergic (AR) and serotonin (5-HT) receptors, we found that adrenoceptor α 2C (Adra2c) and serotonin receptor 2a (Htr2a) were the most highly expressed. Using a mouse model of Stargardt disease, we found that pharmacological interventions that targeted both GPCR signaling pathways and adenylate cyclases (ACs) improved photoreceptor cell survival, preserved photoreceptor function, and attenuated the accumulation of pathological fluorescent deposits in the retina. These findings demonstrate a strategy for the identification of new drug candidates and FDA-approved drugs for the treatment of monogenic and complex diseases.

PMID: 24231350 [PubMed - as supplied by publisher]

Epidemiology

JAMA Ophthalmol. 2013 Nov 14. doi: 10.1001/jamaophthalmol.2013.5696. [Epub ahead of print]

Associations Between Age-Related Macular Degeneration, Alzheimer Disease, and Dementia: Record Linkage Study of Hospital Admissions.

Keenan TD, Goldacre R, Goldacre MJ.

Centre for Hearing and Vision Research, Institute of Human Development, University of Manchester, Manchester, England.

IMPORTANCE: The potential association between age-related macular degeneration (AMD) and Alzheimer disease (AD) is uncertain and has implications for understanding disease pathogenesis, referral, and treatments.

OBJECTIVES: To determine whether individuals admitted to the hospital with AMD were significantly more or less likely to develop AD or dementia in the following years, as well as to assess whether people with AD or dementia were significantly more or less likely to be admitted to the hospital for AMD treatment in the years following diagnosis of dementia.

DESIGN, SETTING, AND PARTICIPANTS: An AMD cohort of 65 894 people was constructed from English National Health Service, linked hospital episode statistics from January 1, 1999, through February 28, 2011, by identifying computerized record abstracts for all people with an admission or day case care for AMD. A dementia cohort (168 092 people) and a reference cohort (>7.7 million people) were constructed in similar ways.

MAIN OUTCOMES AND MEASURES: Risk of AD or dementia following AMD and risk of AMD following AD or dementia. Rate ratios were calculated based on standardized rates of AD and dementia in the AMD cohort, as well as standardized rates of AMD in the AD and dementia cohort, relative to those in the reference cohort.

RESULTS: The risk of AD or dementia following AMD was not elevated. The rate ratio was 0.86 (95% CI, 0.67-1.08) for AD and 0.91 (0.79-1.04) for dementia. The likelihood of being admitted for AMD following AD or dementia was very low: the rate ratio was 0.04 (0.01-0.10) for people with AD and 0.07 (0.04-0.11) for those with dementia.

CONCLUSIONS AND RELEVANCE: These neurodegenerative conditions may share environmental risk factors and histopathologic features. However, considering AD and other dementia after AMD, their coexistence at the individual level is no different from that expected by chance. Our data also suggest that patients in England with dementia may be substantially less likely to receive AMD treatment. Further research is required to determine whether people with dementia receive appropriate investigation and treatment for AMD, as well as identify and address potential barriers.

PMID: 24232933 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2013 Nov 14. pii: iovs.13-13248v1. doi: 10.1167/iovs.13-13248. [Epub ahead of print]

Allergy is a protective factor against age-related macular degeneration.

Ristau T, Ersoy L, Lechanteur YT, den Hollander AI, Daha M, Hahn M, Hoyng CB, Fauser S.

University of Cologne, Cologne, 50924, Germany.

Purpose: To investigate the role of allergy on age-related macular degeneration (AMD).

Methods: AMD staging was performed for 3585 individuals (1878 from Cologne, Germany and 1707 from Nijmegen, the Netherlands). Interviewer-assisted questionnaires were evaluated for the factors smoking, use of corticosteroids, and history of allergy including causative allergens. Serum complement component C3d and C3 levels were measured and the C3d/C3 ratio was calculated. Associations of allergy with AMD/ late AMD were assessed by logistic regression analysis, C3d/C3 ratio was compared between groups.

Results: The discovery cohort from Cologne included 864 AMD patients and 1014 controls; 495 patients had late AMD. Positive history of allergy showed strong protective effects on the phenotype AMD (OR 0.52; p=3.42x10-9) and late AMD (OR 0.32; p=2.57x10-13). Subclassification in allergy-provoking agents showed significant protective effects in all groups. After adjustment for age, gender, smoking, and corticosteroid use, protective effects for AMD (OR 0.75; p=0.018) and late AMD (OR 0.49; p=2.87x10-5) were confirmed. While C3d/C3 ratio was higher in AMD/late AMD patients (both p<0.001), there was no association with allergy in AMD (p=0.22). The protective effect of allergy on AMD was confirmed in the replication cohort from Nijmegen (p=0.002 for AMD; p=0.0001 for late AMD).

Conclusions: Allergy has a protective effect on the development of AMD independent of the provoking allergen, which cannot be explained by complement activation. Further investigations are necessary to elucidate the molecular mechanisms underlying the protective effect of allergy on AMD.

PMID: 24235017 [PubMed - as supplied by publisher]

PLoS One. 2013 Oct 21;8(10):e76770. doi: 10.1371/journal.pone.0076770.

Pseudoexfoliation: normative data and associations. The central India eye and medical study.

Jonas JB, Nangia V, Matin A, Bhojwani K, Sinha A, Khare A, Agarwal S, Bhate K.

Suraj Eye Institute, Nagpur, India ; Department of Ophthalmology, Medical Faculty Mannheim of the Ruprecht-Karls-University Heidelberg, Mannheim, Germany.

PURPOSE: To assess the prevalence of pseudoexfoliation (PEX) and its associations in a population-based setting.

DESIGN: Population-based, cross-sectional study.

METHODS: The Central India Eye and Medical Study included 4711 individuals. All study participants underwent a detailed ophthalmological examination. After medical pupil dilation, PEX was assessed by an experienced ophthalmologist using slit-lamp based biomicroscopy.

RESULTS: Slit lamp examination results were available for 4646 (98.6%) study participants with a mean age of 49.3±13.3 years (range: 30-100 years). PEX was detected in 87 eyes (prevalence: 0.95±0.10% (95%CI: 0.75, 1.15) of 69 subjects (prevalence: 1.49±0.18% (95%CI: 1.14, 1.83). PEX prevalence increased significantly (P<0.001) from 0% in the age group of 30-39 years, to 2.85±0.56% in the age group of 60-69 years, to 6.60±1.21% in the age group of 70-79 years, and to 12.3±4.11% in the age group of 80+ years. In multivariate analysis, PEX prevalence was associated with higher age (P<0.001; regression coefficient B:0.11; odds ratio (OR): 1.11 (95%CI: 1.09, 1.13)), lower body mass index (P=0.001; B: -0.12; OR: 0.88 (95CI: 0.82, 0.95)) and higher diastolic blood pressure (P=0.002; B: 0.02; OR: 1.03 (95%CI: 1.01, 1.04)). In the multivariate analysis, PEX was not associated with retinal nerve fiber layer cross section area (P=0.76) and presence of open-angle glaucoma (P=0.15).

CONCLUSIONS: In a rural Central Indian population aged 30+ years, PEX prevalence (mean: 1.49±0.18%) was significantly associated with older age, lower body mass index and higher diastolic blood pressure. It was not significantly associated with optic nerve head measurements, refractive error, any ocular biometric parameter, nuclear cataract, early age-related macular degeneration and retinal vein occlusion, diabetes mellitus, smoking, and dyslipidemia.

PMID: 24204672 [PubMed - in process] PMCID: PMC3804587

Invest Ophthalmol Vis Sci. 2013 Nov 7. pii: iovs.13-13096v1. doi: 10.1167/iovs.13-13096. [Epub ahead of print]

Prevalence and Risk Factors of Age-Related Macular Degeneration in Korea: The Korean National Health and Nutrition Examination Survey.

Cho BJ, Heo JW, Kim TW, Ahn J, Chung H.

Department of Ophthalmology, Seoul National University College of Medicine, Seoul, 110-744, Korea (South), Republic of.

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

Methods: The study involved a nationally representative Korean population from the 2010-2011 Korean National Health and Nutrition Examination Survey. A total of 7899 subjects aged ≥40 years participated in health interviews, physical examinations, and ophthalmologic assessment including fundus photography.

Results: The overall prevalence of early AMD was estimated at 6.7% (95% confidence interval [CI], 6.1-7.4), and that of late AMD was estimated at 0.7% (95% CI, 0.5-0.9), which included 0.5% prevalence of neovascular AMD and 0.2% prevalence of geographic atrophy. The prevalence rates of early and late AMD among participants aged ≥65 years were 16.9% and 1.8%, respectively. Hyperopia was positively associated with the presence of any AMD type (odds ratio [OR], 1.08 for every 1 diopter increase). In multivariate analyses, significant risk factors for the presence of any AMD type were age, serum high-density lipoprotein (HDL) level, serum gamma-glutamyl transferase (GGT) level, and hepatitis B surface antigen (HBsAg) serum positivity (OR, 2.26). The risk factors for late AMD included age, ever smoking history (OR, 2.18), serum GGT level, and systolic blood pressure.

Conclusions: The prevalence of AMD in Korea was similar to the prevalence of pooled Asian and Western populations. Age and serum GGT level were strongly associated with both the presence of any AMD and late AMD. Additionally, serum HDL level, HBsAg serum positivity, ever smoking history, and systolic blood pressure were identified as risk factors for AMD.

PMID: 24204048 [PubMed - as supplied by publisher]

Genetics

Saudi J Ophthalmol. 2013 Apr;27(2):107-111. Epub 2013 Feb 11.

The gene therapy revolution in ophthalmology.

Al-Saikhan FI.

College of Pharmacy, Salman Bin Abdulaziz University, Al-Kharj, Saudi Arabia.

Abstract: The advances in gene therapy hold significant promise for the treatment of ophthalmic conditions. Several studies using animal models have been published. Animal models on retinitis pigmentosa, Leber's Congenital Amaurosis (LCA), and Stargardt disease have involved the use of adeno-associated virus (AAV) to deliver functional genes into mice and canines. Mice models have been used to show that a mutation in cGMP phosphodiesterase that results in retinitis pigmentosa can be corrected using rAAV vectors. Additionally, rAAV vectors have been successfully used to deliver ribozyme into mice with a subsequent improvement in autosomal dominant retinitis pigmentosa. By using dog models, researchers have made progress in studying X-linked retinitis pigmentosa which results from a RPGR gene mutation. Mouse and canine models have also been used in the study of LCA. The widely studied form of LCA is LCA2, resulting from a mutation in the gene RPE65. Mice and canines that were injected with normal copies of RPE65 gene showed signs such as improved retinal pigment epithelium transduction, visual acuity, and functional recovery. Studies on Stargardt disease have shown that mutations in the ABCA4 gene can be corrected with AAV vectors, or nanoparticles. Gene therapy for the treatment of red-green color blindness was successful in squirrel monkeys. Plans are at an advanced stage to begin clinical trials. Researchers have also proved that CD59 can be used with AMD. Gene therapy is also able to treat primary open angle glaucoma (POAG) in animal models, and studies show it is economically viable.

PMID: 24227970 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2013 Nov 14. pii: iovs.13-12867v1. doi: 10.1167/iovs.13-12867. [Epub ahead of print]

TNFRSF10A-LOC389641 rs13278062 but not REST-C4orf14 - POLR2B-IGFBP7 rs1713985 was found associated with Age-Related Macular Degeneration in a Chinese Population.

Sun Y, Li S, Li H, Yang F, Bai Y, Zhao M, Guo J, Zhao M, Zhou P, Khor CC, Huang L, Li X.

Ophthalmology, Peking University People's Hospital, Beijing, 100044, China.

Purpose: To reassess the association between TNFRSF10-LOC389641 rs13278062 and REST-C4orf14-POLR2B-IGFBP7 rs1713985 with the risk of age-related macular degeneration (AMD) in a Chinese case-control collection

Methods: The primary study consisted of 1,826 subjects, including 1,226 controls, 300 cases with nAMD, and 300 cases with PCV. Genomic DNA was extracted from venous blood leukocytes. The allelic variants of rs13278062 and rs1713985 were determined by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. The difference in allele distribution between cases and controls was tested using a $\chi 2$

test.We also performed a meta-analysis of case-control studies for rs13278062 and rs1713985 in Hong Kong and Singaporean late AMD collections of Chinese descent (1,273 cases and 1,652 controls) via an inverse-variance, fixed effects model as previously described. Subgroup analysis of CNV and PCV subtypes were also performed.

Results: We found no evidence to support a significant association of markers rs13278062 or rs1713985 with neither nAMD nor PCV, nor total AMD in our Beijing study (P>0.05 for all comparisons). Upon meta-analysis of all sample collections, we note nominally significant association between rs13278062 and increased risk of late AMD, consistent with previous findings in Japanese (ORmeta =1.17, Pmeta = 0.004). No association was detected between rs1713985 and AMD when all data were meta-analyzed.

Conclusions: SNP rs13278062, but not rs1713985 showed nominal evidence of association with AMD in a total of 1,273 cases and 1,652 controls of Chinese descent. The difference between different effect sizes in our study and others'suggested that future studies with much larger sample sizes is necessary.

PMID: 24235014 [PubMed - as supplied by publisher]

Diet & lifestyle

PLoS One. 2013 Nov 6;8(11):e79848. doi: 10.1371/journal.pone.0079848.

Association of HDL-Related Loci with Age-Related Macular Degeneration and Plasma Lutein and Zeaxanthin: the Alienor Study.

Merle BM, Maubaret C, Korobelnik JF, Delyfer MN, Rougier MB, Lambert JC, Amouyel P, Malet F, Le Goff M, Dartigues JF, Barberger-Gateau P, Delcourt C.

INSERM, (Institut National de la Santé et de la Recherche Médicale), ISPED (Institut de Santé Publique d'Épidémiologie et de Développement), Centre INSERM U897-Epidemiologie-Biostatistique, Bordeaux, France ; Université de Bordeaux, Bordeaux, France.

BACKGROUND: Several genes implicated in high-density lipoprotein (HDL) metabolism have been reported to be associated with age-related macular degeneration (AMD). Furthermore, HDL transport the two carotenoids, lutein and zeaxanthin, which are highly suspected to play a key-role in the protection against AMD. The objective is to confirm the associations of HDL-related loci with AMD and to assess their associations with plasma lutein and zeaxanthin concentrations.

METHODS: Alienor study is a prospective population-based study on nutrition and age-related eye diseases performed in 963 elderly residents of Bordeaux, France. AMD was graded according to the international classification, from non-mydriatic colour retinal photographs. Plasma lutein and zeaxanthin were determined by normal-phase high-performance liquid chromatography. The following polymorphisms were studied: rs493258 and rs10468017 (LIPC), rs3764261 (CETP), rs12678919 (LPL) and rs1883025 (ABCA1).

RESULTS: After multivariate adjustment, the TT genotype of the LIPC rs493258 variant was significantly associated with a reduced risk for early and late AMD (OR=0.64, 95%CI: 0.41-0.99; p=0.049 and OR=0.26, 95%CI: 0.08-0.85; p=0.03, respectively), and with higher plasma zeaxanthin concentrations (p=0.03), while plasma lipids were not significantly different according to this SNP. Besides, the LPL variant was associated with early AMD (OR=0.67, 95%CI: 0.45-1.00; p=0.05) and both with plasma lipids and plasma lutein (p=0.047). Associations of LIPC rs10468017, CETP and ABCA1 polymorphisms with AMD did not reach statistical significance.

CONCLUSION: These findings suggest that LIPC and LPL genes could both modify the risk for AMD and the metabolism of lutein and zeaxanthin.

PMID: 24223199 [PubMed - in process] PMCID: PMC3819249

Consult Pharm. 2013 Nov 1;28(11):723-37. doi: 10.4140/TCP.n.2013.723.

Prevention and treatment of age-related macular degeneration: an update for pharmacists.

Marshall LL, Roach JM.

Mercer University College of Pharmacy, Atlanta, Georgia.

Objective: Review the current recommendations for the prevention and treatment of age-related macular degeneration (AMD).

Data Sources: Articles indexed in PubMed (National Library of Medicine), the Cochrane Reviews and Trials, Dynamed, and Iowa Drug Information Service (IDIS) in the last 10 years using the key words macular degeneration, agerelated macular degeneration (AMD), AMD and treatment, AMD and prevention.

Study Selection and Data Extraction: Sixty-nine published papers were reviewed, and criteria supporting the primary objective were used to identify useful resources.

Data Synthesis: The literature included practice guidelines, original research articles, review articles, product prescribing information, and supplement product information for the prevention and treatment of AMD.

Conclusion: AMD is a leading cause of visual impairment in older adults. At present there is no cure for advanced AMD, but intravitreal vascular endothelial growth factor inhibitors minimize and even reverse vision loss in patients with AMD of the neovascular type. In the Age-Related Eye Disease Study (AREDS), participants with intermediate AMD who received a supplement combination of vitamins C and E, beta-carotene, and zinc had a greater delay in progression to advanced AMD than those participants who received a portion of these supplements. In the second AREDS, AREDS2, the addition of lutein + zeaxanthin, docosahexaenoic acid (DHA) + eicosapentaenoic acid (EPA), or lutein + zeaxanthin and DHA + EPA to the complete AREDS formulation did not further reduce the risk of progression to advanced AMD. Subgroup analyses indicated that additional research with lutein + zeaxanthin supplementation is warranted as it was beneficial in participants with low dietary intake of lutein + zeaxanthin. A formulation without beta-carotene may be best for most patients, especially smokers or former smokers. Health care professionals will want to consider patient-specific information before recommending ocular health supplements.

PMID: 24217192 [PubMed - in process]

Eye (Lond). 2013 Nov 8. doi: 10.1038/eye.2013.239. [Epub ahead of print]

Activation of the mitochondrial caspase pathway and subsequent calpain activation in monkey RPE cells cultured under zinc depletion.

Nakajima E, Hammond KB, Shearer TR, Azuma M.

1] Senju Laboratory of Ocular Sciences, Senju Pharmaceutical Corporation Limited, Portland, OR, USA [2] Department of Integrative Biosciences, Oregon Health & Science University, Portland, OR, USA.

Purpose: Decreased zinc levels in the macula are reported in patients with age-related macular degeneration, and the zinc chelator N,N,N',N'-tetrakis (2- pyridylmethyl) ethylenediamine) (TPEN) causes death of human retinal pigment epithelial (RPE) cells. The purpose of the present study was to investigate signal transduction pathways during cell death initiated by TPEN, using monkey RPE cells.

Methods: RPE cells were cultured with TPEN. Activation of calpains and caspases, and proteolysis of their substrates were detected by immunoblotting. Incubation of calpain inhibitor SNJ-1945 or caspase inhibitor z -VAD-fmk was used to confirm activation of specific proteases.

Results: TPEN caused a time-dependent decrease in viable RPE cells. Cell death was accompanied by

activation of calpain-1, caspase-9, and caspase-3. SNJ-1945 inhibited calpain activation and slightly inhibited caspase-9 activation. z-VAD-fmk inhibited caspases and calpain-1 activation. TPEN did not activate caspase-12.

Conclusions: Relative zinc deficiency in RPE cells causes activation of cytosolic calpain and mitochondrial caspase pathways without ER stress.

PMID: 24202052 [PubMed - as supplied by publisher]

Am J Clin Nutr. 2013 Oct;98(4):1144. doi: 10.3945/ajcn.113.071142

Kawada T

Comment on Homocysteine, folate, vitamin B-12, and 10-y incidence of age-related macular degeneration. [Am J Clin Nutr. 2013]

Nutrients related to the incidence of early and late age-related macular degeneration.

Am J Clin Nutr. 2013 Oct;98(4):1144-5. doi: 10.3945/ajcn.113.071746.

Gopinath B, Flood VM, Mitchell P.

Reply to Kawada.