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MD Research News

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Drug treatment

Eur J Ophthalmol. 2013 Mar 20:0. doi: 10.5301/ejo.5000268. [Epub ahead of print]

The results of switching between 2 anti-VEGF drugs, bevacizumab and ranibizumab, in the treatment of neovascular age-related macular degeneration.

Aslankurt M, Aslan L, Aksoy A, Erden B, Cekiç O.

Department of Ophthalmology, Kahramanmaras Sutcu Imam University, Kahramanmaras - Turkey.

Purpose: To report the results of switching from intravitreal bevacizumab to ranibizumab or vice versa in the treatment of choroidal neovascularization (CNV) due to age-related macular degeneration.

Methods: Twenty eyes of 18 patients that underwent switch from intravitreal bevacizumab to ranibizumab and 10 eyes of 8 patients that underwent switch from ranibizumab to bevacizumab were retrospectively analyzed. The results were compared with 41 eyes of 37 patients treated with ranibizumab only. All eyes initially received 3 injections of ranibizumab or bevacizumab, which were repeated as needed (PRN dosing). Anti-vascular endothelial growth factor therapies were switched because of general health insurance applications and cost problems. The main outcome measures were best-corrected visual acuity (BCVA), injection number, and central macular thickness (CMT) obtained by optical coherence tomography.

Results: Once all patients evaluated together at the final visit, the mean BCVA improved and CMT decreased. When switching groups were taken into consideration, switching yielded improved BCVA and reduced CMT following switching. After switching, BCVA continuously improved in the bevacizumab to ranibizumab group, but stayed stable in the ranibizumab to bevacizumab group. The CMT was reduced at the switching time in both groups, but did not change after the switch. Final visual acuity improved or stabilized in all eyes in the ranibizumab-only group. The BCVA worsened in 20% of eyes in the bevacizumab to ranibizumab group and in 40% of eyes in the ranibizumab to bevacizumab group.

Conclusion: The ranibizumab-only group and the switching from bevacizumab to ranibizumab group seemed superior to the ranibizumab to bevacizumab group.

PMID: 23516253 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2013;7:495-501. doi: 10.2147/OPTH.S29974. Epub 2013 Mar 8.

Comparative effectiveness of aflibercept for the treatment of patients with neovascular age-related macular degeneration.

Thomas M, Mousa SS, Mousa SA.

Pharmaceutical Research Institute, Albany College of Pharmacy and Health Sciences, Albany, NY, USA.

Abstract: Wet age-related macular degeneration (AMD) is the most common reason for vision loss in the United States. Many treatments, such as laser therapy and photodynamic therapies, have been used but their efficacy is limited. Emerging anti-vascular endothelial growth factor (VEGF) therapies are now considered the standard of care. Anti-VEGF agents inhibit angiogenesis in the eye by suppressing abnormal blood vessel growth, leading to vision improvement. Ranibizumab and bevacizumab are two examples of anti-VEGF drugs that have been approved; both showed promise based on the visual acuity scale. Aflibercept, another new therapy known to trap VEGF and inhibit multiple growth factors, is promising not only because it can be taken bimonthly based on year 1 of the VIEW trials, but it can also be extended, as demonstrated in year 2 of the VIEW trials. Based on a cost-effect analysis, aflibercept is comparable to other leading therapies. This is a review of relevant clinical trials that have proven the non-inferiority and safety of aflibercept compared to the standard of care and its unique role in the current management of wet AMD.

PMID: 23503202 [PubMed] PMCID: PMC3595183

Am J Ophthalmol. 2013 Mar 13. pii: S0002-9394(13)00071-8. doi: 10.1016/j.ajo.2013.01.015. [Epub ahead of print]

16 and 24 Gy Low-voltage X-ray Irradiation With Ranibizumab Therapy for Neovascular Age-Related Macular Degeneration: 12-Month Outcomes.

Morales-Canton V, Quiroz-Mercado H, Velez-Montoya R, Zavala-Ayala A, Moshfeghi AA, Shusterman EM, Kaiser PK, Sanislo SR, Gertner M, Moshfeghi DM.

Associacion Para Evitar La Ceguera En Mexico, I.A.P., Mexico City, Mexico.

PURPOSE: To describe the 12-month safety and efficacy outcomes of 16 or 24 Gy radiation using low-voltage x-ray irradiation in conjunction with intravitreal ranibizumab for neovascular age-related macular degeneration (AMD).

DESIGN: Prospective, phase I, open-label, nonrandomized uncontrolled safety study.

METHODS: setting: Institutional. study population: Neovascular AMD patients. intervention: One x-ray irradiation treatment at 16 or 24 Gy was administered externally through 3 locations in the inferior pars plana. After 2 initial monthly loading doses of ranibizumab, subsequent ranibizumab was administered according to predetermined criteria. main outcome measures: Visual acuity, number of ranibizumab injections, safety and efficacy metrics at 12 months.

RESULTS: Forty-seven eyes of 47 patients were enrolled and completed 12 months of follow-up: 16 Gy (n = 28) and 24 Gy (n = 19). There was no evidence of radiation retinopathy, optic neuropathy, or cataract. The mean visual acuity improved in both groups: +8.4 ± 11.9 letters and +7.8 ± 12 letters for 16 and 24 Gy, respectively. In both groups, 100% of subjects lost <15 letters, with 76% and 79% gaining ≥0 letters in the 16 Gy and 24 Gy groups, respectively. Patients received a mean of 1.0 additional injection over 12 months. The mean change in optical coherence tomography central subfield thickness from baseline to month 12 was -107 and -87 μm for the 16 Gy and 24 Gy groups, respectively.

CONCLUSION: One treatment of 16 or 24 Gy low-voltage x-ray therapy with as-needed ranibizumab appears safe in subjects with neovascular AMD at 12 months. An overall improvement in visual acuity was observed. No radiation-related adverse effects were reported.

PMID: 23497847 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging Retina. 2013 Mar 1;44(2):121-6. doi: 10.3928/23258160-20130313-04.

SAVE (Super-dose Anti-VEGF) Trial: 2.0 mg Ranibizumab for Recalcitrant Neovascular Age-Related

Macular Degeneration: 1-Year Results.

Wykoff CC, Brown DM, Chen E, Major JC, Croft DE, Mariani A, Wong TP; SAVE Study Group.

OBJECTIVES: To assess durability of visual and anatomic gains with 2.0 mg ranibizumab in recalcitrant neovascular age-related macular degeneration (AMD).

METHODS: Phase I-II trial of 88 patients with recalcitrant neovascular AMD treated as needed every 4 (cohort A) or 6 weeks (cohort B) following three monthly doses. ETDRS refraction and spectral-domain OCT-guided as-needed re-treatments.

RESULTS: Seventy-nine patients completed the 12-month endpoint and were given 11.6 (cohort A) and 8.6 (cohort B) mean treatments. Mean best corrected visual acuity gains of 4.1 letters following three monthly doses were sustained for 12 months for both cohorts. Anatomic improvements were sustained for 12 months for cohort A, but not for cohort B; cohort B demonstrated a gradual increase in mean central retinal thickness (P = .03).

CONCLUSION: Visual and anatomic gains achieved with 2.0 mg ranibizumab in recalcitrant neovascular AMD were sustained for 1 year with monthly treatment. In comparison, anatomic gains were diminished with less than monthly treatment.[Ophthalmic Surg Lasers Imaging Retina. 2013;44:121-126].

PMID: 23510037 [PubMed - in process]

Med J Aust. 2013 Mar 18;198(5):260-1.

Antivascular endothelial growth factor treatments for neovascular age-related macular degeneration save sight, but does everyone get treated?

Finger RP, Guymer RH.

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PMID: 23496400 [PubMed - in process]

Ophthalmic Surg Lasers Imaging Retina. 2013 Mar 1;44(2):109. doi: 10.3928/23258160-20130313-01.

Recalcitrant Neovascular Macular Degeneration After Anti-VEGF Therapy: An Ongoing Challenge.

Puliafito CA.

Abstract: This editorial describes the challenge of managing eyes that demonstrate signs of persistent exudation after anti-VEGF treatment and illuminates the significance of a new report of using high-dose ranibizumab in treating recalcitrant neovascular age-related macular degeneration.

PMID: 23510034 [PubMed - in process]

Clin Ophthalmol. 2013;6:533-43. doi: 10.2147/OPTH.S31016. Epub 2013 Mar 13.

Emerging roles for antiangiogenesis factors in management of ocular disease.

Saeed MU, Gkaragkani E, Ali K.

The Sutton Eye Unit, Epsom and St Helier's University Hospitals NHS Trust, London, UK.

Abstract: The first antivascular endothelial growth factor (anti-VEGF) was developed as an anticancer drug for colonic carcinomas. Since then, anti-VEGFs have developed in scope and indications. They have revolutionized the treatment of exudative macular degeneration and have had a major impact on treatment of

several other conditions. This has resulted in an increased number of patients seeking treatment with new treatment options and has had a considerable financial impact on health care resources. Anti-VEGFs have been used in the treatment of all age groups of the population ranging from infants where it is used for treatment of retinopathy of prematurity to the elderly where it is used in exudative macular eegeneration.

PMID: 23515639 [PubMed]

Retina. 2013 Mar 19. [Epub ahead of print]

INTRAVITREAL ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR FOR CHOROIDAL NEOVASCULARIZATION SECONDARY TO PATHOLOGIC MYOPIA: Systematic Review and Meta-Analysis.

Wang E, Chen Y.

Department of Ophthalmology, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing, China.

PURPOSES: To update existing evidence and evaluate intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections for myopic choroidal neovascularization.

METHODS: The authors conducted comprehensive search in PubMed, EMBASE, Cochrane Library, Biosis Preview, and LILACS. Included studies were categorized by study design. Comparative studies were classified as randomized controlled trials (RCTs) and non-RCT studies, and these two types of studies were presented and meta-analyzed separately for the following comparisons: 1) anti-VEGF versus photodynamic therapy, 2) anti-VEGF monotherapy versus combination therapy with photodynamic therapy, 3) single versus 3 monthly injections followed by pro re nata (PRN) treatment, and 4) ranibizumab versus bevacizumab. Noncomparative prospective series were pooled to estimate mean visual gain, mean retinal thickness change, and the average number of anti-VEGF injections required for myopic choroidal neovascularization. Ocular and systemic adverse events were also summarized.

RESULTS: Literature search yielded 18 comparative studies and 83 noncomparative studies. Superiority of anti-VEGF over photodynamic therapy in a 24-month period was confirmed by 2 RCTs and 6 non-RCT studies. The influence of combined photodynamic therapy was uncertain based on two non-RCT studies. Three non-RCT studies showed that the visual outcomes of 3+PRN injections might be slightly better than 1+PRN injections within 1 year. No difference was observed between ranibizumab and bevacizumab in two RCTs and one non-RCT study. The estimated visual improvement was two lines on average. Adverse events were uncommon as reported.

CONCLUSION: Accumulating evidence confirmed that anti-VEGF injections should be the first-line therapy for myopic choroidal neovascularization.

PMID: 23514793 [PubMed - as supplied by publisher]

Curr Opin Ophthalmol. 2013 Mar 20. [Epub ahead of print]

Corticosteroid intravitreal implants vs. ranibizumab for the treatment of vitreoretinal disease.

Comyn O, Lightman SL, Hykin PG.

aNIHR Biomedical Research Centre bMedical Retina Department cMoorfields Eye Hospital NHS Foundation Trust dUCL Institute of Ophthalmology, London, UK.

PURPOSE OF REVIEW: Three long-acting corticosteroid implants are now available for the treatment of retinal disease, offering control of macular edema and inflammation for between 6 months and up to 3 years. This review evaluates their efficacy and side-effect profile in comparison with the antivascular endothelial growth factor agent ranibizumab in diabetic macular edema, retinal vein occlusion, pseudophakic macular edema, and uveitis.

RECENT FINDINGS: Trials of ranibizumab in diabetic macular edema have demonstrated excellent efficacy without serious safety concerns to date. Fluocinolone acetonide implants can be considered, but have a high risk of cataract and sequelae from intraocular pressure rise. In retinal vein occlusion, both ranibizumab and Ozurdex have been shown to be effective, although their relative efficacy has not been determined in head-to-head clinical trials. In pseudophakic and uveitic macular edema, steroid implants are probably the first choice therapy, although there is evidence that ranibizumab is effective. For choroidal neovascularization secondary to inflammatory disease, ranibizumab is indicated, whereas Retisert has been shown to reduce the risk of uveitis relapse.

SUMMARY: In diabetic macular edema, ranibizumab has shown greater efficacy with fewer side-effects than steroid implants. Both ranibizumab and steroid implants can be considered in retinal vein occlusion, but trials are awaited to determine their relative efficacy.

PMID: 23518614 [PubMed - as supplied by publisher]

Curr Opin Ophthalmol. 2013 Mar 20. [Epub ahead of print]

Ocular and systemic safety of bevacizumab and ranibizumab in patients with neovascular age-related macular degeneration.

Johnson D, Sharma S.

Department of Ophthalmology, Queen's University Kingston, Ontario, Canada.

PURPOSE OF REVIEW: This study reviews differences in both ocular and systemic safety between intravitreal bevacizumab and ranibizumab in the setting of neovascular age-related macular degeneration.

RECENT FINDINGS: Serious adverse events associated with either bevacizumab and ranibizumab injections are generally rare. However, acute intraocular inflammation (AII) tends to occur more frequently following bevacizumab injection. Systemic absorption of bevacizumab is greater than with ranibizumab, and many studies have shown an increased risk of systemic adverse events in patients receiving bevacizumab compared with those receiving ranibizumab.

SUMMARY: Although rare, adverse events with off-label use of bevacizumab are more common than with ranibizumab. Continued study into long-term safety of the two agents is warranted.

PMID: 23518613 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2013 Mar;230(3):247-54. doi: 10.1055/s-0032-1328161. Epub 2013 Mar 18.

[Multikinase Inhibitors as a New Approach in Neovascular Age-Related Macular Degeneration (AMD) Treatment: In Vitro Safety Evaluations of Axitinib, Pazopanib and Sorafenib for Intraocular Use]. [Article in German]

Thiele S, Liegl RG, König S, Siedlecki J, Langer J, Eibl K, Haritoglou C, Kampik A, Kernt M.

Augenklinik, Ludwig-Maximilians-Universität München.

Background: Multikinase inhibitors (MKI) interfere effectively at different levels of the neovascularisation cascade. Early clinical and experimental data suggest that MKIs represent a promising novel approach for the treatment of neovascular age-related macular degeneration (AMD). However, so far little is known about the biocompatibility of MKIs regarding human ocular cells. This in vitro study investigates and compares the biocompatibility of three MKIs, axitinib, pazopanib, and sorafenib regarding ocular cells of the anterior and posterior segments, as well as organ-cultured donor corneas.

Methods: Primary human optic nerve head astrocytes (ONHA), trabecular meshwork cells (TMC), and retinal pigment epithelium (RPE), human corneal endothelial and lens epithelial cells (CEC and LEC) were

treated with different concentrations of axitinib, pazopanib, or sorafenib (0.1 to 100 µg/mL). To simulate oxidative stress, the cells were additionally co-incubated with 400 µM hydrogen peroxide. Induction of cell death and cellular viability were examined by live-dead assay and tetrazolium dye reduction assay (MTT). In addition, the influence of the three substances on human corneal endothelium was evaluated in sero-positive donor corneas in organ culture by phase contrast microscopy.

Results: Up to a concentration of 7.5 mg/mL of the substances tested in any cell type examined, no toxic effects were found. Even after 10 days of incubation of organ-cultured donor corneas with 7.5 µg/mL, axitinib, pazopanib, or sorafenib, no evidence for endothelial toxicity was found.

Conclusion: All three MKIs tested, axitinib, pazopanib, and sorafenib showed a good biocompatibility on the investigated ocular cells. Even under conditions of oxidative stress, there were no toxic effects up to a concentration of 7.5 µg/mL. Only at higher concentrations, there was a dose-dependent decrease in cellular viability and pronounced induction of cell death. These effects on cellular viability and induction of cell death appeared to be stronger with pazopanib, followed by sorafenib, than with axitinib.

PMID: 23508753 [PubMed - in process]

Other treatment & diagnosis

PLoS One. 2013;8(3):e58821. doi: 10.1371/journal.pone.0058821. Epub 2013 Mar 14.

Aspirin use and risk of age-related macular degeneration: a meta-analysis.

Zhu W, Wu Y, Xu D, Li YH, Jun B, Zhang XL, Wang F, Yu J.

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BACKGROUND: Age-related macular degeneration (AMD) is the main cause of blindness and the curative options are limited. The objective of this meta-analysis was to determine the association between aspirin use and risk of AMD.

METHODS: A comprehensive literature search was performed in PubMed, Embase, Web of Science, and reference lists. A meta-analysis was performed by STATA software.

RESULTS: Ten studies involving 171729 individuals examining the association between aspirin use and risk of AMD were included. Among the included studies, 2 were randomized-controlled trials (RCTs), 4 were case-control studies and 4 were cohort studies. The relative risks (RRs) were pooled using a random-effects model. Relative risks with 95% confidence intervals (CIs) of aspirin use as a risk for AMD. The pooled RR of 10 included studies between the use of aspirin and risk of AMD was 1.09 (95% CI, 0.96-1.24). The same result was detected in early and late stage AMD subgroup analysis. In the subgroup analyses, the pooled RR of RCTs, case-control studies and cohort studies were 0.81 (95% CI, 0.64-1.02), 1.02 (95% CI, 0.92-1.14) and 1.08 (95% CI, 0.91-1.28), respectively.

CONCLUSIONS: The use of aspirin was not associated with the risk of AMD.

PMID: 23516561 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2013 Mar 21. pii: iovs.13-11825v1. doi: 10.1167/iovs.13-11825. [Epub ahead of print]

Mobility Experiments with Microrobots for Minimally Invasive Intraocular Surgery.

Ullrich F, Bergeles C, Pokki J, Ergeneman O, Erni S, Chatzipirpiridis G, Pane S, Framme C, Nelson BJ.

Institute of Robotics and Intelligent Systems, ETH Zurich, Zurich, 8092, Switzerland.

PURPOSE: To investigate microrobots as an assistive tool for minimally invasive intraocular surgery and to

demonstrate mobility and controllability inside the living rabbit eye.

METHODS: A system for wireless magnetic control of untethered microrobots was developed. Mobility and controllability of a microrobot are examined in different media, specifically vitreous, balanced salt solution (BSS) and silicone oil. This is demonstrated through ex vivo and in vivo animal experiments.

RESULTS: The developed electromagnetic system enables precise control of magnetic microrobots over a workspace that covers the posterior eye segment. The system allows for rotation and translation of the microrobot in different media (vitreous, BSS, silicone oil) inside the eye.

CONCLUSIONS: Intravitreal introduction of untethered mobile microrobots can enable suture-less and precise ophthalmic procedures. Ex vivo and in vivo experiments demonstrate that microrobots can be manipulated in fluids inside the eye. Potential applications are targeted drug-delivery for maculopathies such as age-related macular degeneration (AMD), intravenous deployment of anti-coagulation agents for retinal-vein occlusion (RVO) and mechanical applications, such as epiretinal membrane peeling (ERM). The technology has the potential to reduce the invasiveness of ophthalmic surgery and assist in the treatment of a variety of ophthalmic diseases.

PMID: 23518764 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging Retina. 2013 Mar 1;44(2):204-7. doi: 10.3928/23258160-20130313-12.

Increasing Volume of a Retinal Pigmented Epithelial Detachment as a Predictor of Submacular Hemorrhage During Anti-VEGF Therapy.

de Amorim Garcia Filho CA, Penha FM, Gregori G, Rosenfeld PJ.

Abstract: Vascularized retinal pigment epithelium detachments (PEDs) are part of the spectrum of neovascular age-related macular degeneration (AMD). These patients with vascularized PEDs are at a higher risk of experiencing severe vision loss. This case report demonstrates the use of a new spectral-domain optical coherence tomography (SD-OCT) algorithm to measure the area and volume of PEDs. When this algorithm was applied to the scans from a patient with a vascularized PED who developed a large submacular hemorrhage while undergoing ranibizumab therapy, the authors found that the algorithm measured an increase in the area and volume of the PED that preceded the macular hemorrhage. Although further studies are needed, the increase in the volume of a PED may serve as a useful predictor of disease progression and the need for more aggressive anti-VEGF therapy.[Ophthalmic Surg Lasers Imaging Retina. 2013;44:204-207].

PMID: 23510045 [PubMed - in process]

Klin Monbl Augenheilkd. 2013 Mar;230(3):270-4. doi: 10.1055/s-0032-1328159. Epub 2013 Mar 18.

[Predictive Near-Infrared SLO Signs for Tears of the Retinal Pigment Epithelium due to Age-Related Macular Degeneration]. [Article in German]

Bastian N, Fonseca S, Clemens CR, Fleckenstein M, Schmitz-Valckenberg S, Holz FG.

Augenklinik, Universität Bonn.

Purpose: The aim of this study was to identify potential predictive markers in confocal scanning laser ophthalmoscopy (cSLO)-based imaging for tears of the retinal pigment epithelium (RPE) in the presence of pigment epithelial detachments (PED) due to age-related macular degeneration (AMD).

Methods: Fifteen eyes of 15 patients (mean age 77 years, SD ± 6) with RPE tears and pre-existing PEDs were retrospectively analysed for the presence of increased signals on near-infrared imaging (NIR) using confocal scanning laser ophthalmoscopy (cSLO).

Results: In 87 % of the cases increased reflectance signals on NIR in the area of the PED were noted prior to the development of an RPE tear. On average, these signals were recorded 58 days (SD ± 40) before the rip was diagnosed. In 62 % of the patients these signals were localised opposite to the rip location at the rim of the PED.

Conclusion: Increased reflectance signals on NIR imaging may serve as a predictive marker for RPE tears in patients with PED in AMD. These signals recordable with a non-invasive imaging method should be prospectively validated in a larger cohort of patients with PEDs. It may be useful in the management of patients exhibiting this manifestation of exudative AMD.

PMID: 23508756 [PubMed - in process]

Ophthalmic Surg Lasers Imaging Retina. 2013 Mar 1;44(2):127-32. doi: 10.3928/23258160-20130313-05.

Comparison of Geographic Atrophy Measurements from the OCT Fundus Image and the Sub-RPE Slab Image.

Yehoshua Z, Garcia Filho CA, Penha FM, Gregori G, Stetson PF, Feuer WJ, Rosenfeld PJ.

PURPOSE: To compare two different approaches to measuring areas of geographic atrophy (GA) using spectral-domain optical coherence tomography (SD-OCT).

METHODS: Fifty eyes with GA were imaged with an SD-OCT instrument. OCT fundus images and sub-retinal pigment epithelium (RPE) slab images were generated. Three graders manually drew the GA boundaries on both en face images. An automated algorithm was used to segment the GA boundaries from the sub-RPE slabs.

RESULTS: The agreement between the three manual measurements on both OCT fundus images (ICC = .998) and sub-RPE slabs (ICC = .999) was excellent. Area measurements from OCT fundus images and sub-RPE slabs were highly correlated. The agreement between manual and automated measurements on the sub-RPE slabs was very good (ICC = .795).

CONCLUSION: Both OCT fundus images and sub-RPE slab images proved useful for measuring GA in age-related macular degeneration. The automated algorithm typically provided useful measurements of GA area from the sub-RPE slabs.[Ophthalmic Surg Lasers Imaging Retina. 2013;44:127-132].

PMID: 23510038 [PubMed - in process]

Curr Opin Ophthalmol. 2013 Mar 20. [Epub ahead of print]

Detection of new-onset choroidal neovascularization.

Do DV.

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PURPOSE OF REVIEW: To highlight the most common methods that are used to detect new-onset choroidal neovascularization (CNV) as a result of age-related macular degeneration (AMD).

RECENT FINDINGS: Numerous modalities are available to try to detect CNV. Amsler grid testing, preferential hyperacuity perimetry (PHP), optical coherence tomography (OCT), and fluorescein angiography are tools that may be used to detect CNV. The Age-Related Macular Degeneration: Detection of Onset of new Choroidal neovascularization Study (AMD DOC Study) evaluated the sensitivity of time domain OCT, relative to fluorescein angiography, in detecting new-onset neovascular AMD within a 2-year period. The sensitivity of each modality for detecting CNV was OCT 0.40 [(95% confidence interval (95% CI) (0.16-0.68),

supervised Amsler grid 0.42 (95% CI 0.15-0.72), and PHP 0.50 (95% CI 0.23-0.77)].

SUMMARY: Numerous modalities are available to try to detect CNV. The prospective AMD DOC Study demonstrated that fluorescein angiography still remains the best method to detect new-onset CNV.

PMID: 23518615 [PubMed - as supplied by publisher]

Retina. 2013 Mar 20. [Epub ahead of print]

BULLOUS HEMORRHAGIC RETINAL DETACHMENT BECAUSE OF MASSIVE SUBRETINAL HEMORRHAGE IN PATIENTS WITH AGE-RELATED MACULAR DEGENERATION.

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PURPOSE: The authors investigated the surgical outcomes of massive subretinal hemorrhage draining via a retinotomy procedure in bullous hemorrhagic retinal detachment (HRD).

METHODS: Clinical records of consecutive patients with age-related macular degeneration who underwent surgery for bullous HRD were reviewed. Outcomes included anatomical success, visual acuity, and postoperative complications.

RESULTS: Seventeen consecutive eyes of 17 patients were included in this series. Of the 17 eyes, 8 eyes had total HRD and 9 eyes had half total inferior HRD including the macula. The mean interval between initial symptom presentation and operation was 22.6 ± 11.7 days. All patients underwent pars plana vitrectomy and internal drainage of the subretinal hemorrhage through a posterior drainage retinotomy. The mean follow-up period was 37.1 months (range, 12-66 months). Finally, successful retinal reattachment was achieved in 15 of the 17 eyes (88.2%), but 2 remained nonprogressive localized inferior retinal detachment because of proliferative vitreoretinopathy. All preoperative visual acuities were hand movements or worse, and 10 eyes (58.8%) achieved a postoperative minimum functional vision of 20/1000 or better.

CONCLUSION: Successful retinal reattachment and achievement of minimum functional vision is possible after PPV and retinotomy with evacuation of a massive subretinal hemorrhage for bullous HRD secondary to age-related macular degeneration.

PMID: 23518899 [PubMed - as supplied by publisher]

Jpn J Ophthalmol. 2013 Mar 19. [Epub ahead of print]

Visual outcome of photodynamic therapy for typical neovascular age-related macular degeneration and polypoidal choroidal vasculopathy over 5 years of follow-up.

Miki A, Honda S, Kojima H, Nishizaki M, Nagai T, Fujihara M, Uenishi M, Kita M, Kurimoto Y, Negi A; Hyogo Macular Disease Study Group.

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PURPOSE: To evaluate the long-term effects of photodynamic therapy (PDT) on typical neovascular age-related macular degeneration (tAMD) and polypoidal choroidal vasculopathy (PCV).

METHODS: This was a multicenter prospective study of 139 eyes from 136 patients (tAMD: 74 eyes; PCV: 65 eyes) who underwent PDT as the initial treatment. The change in best-corrected visual acuity (BCVA), predictive factors for the BCVA at 60 months, frequency of recurrence, and mean recurrence period were analyzed.

RESULTS: The pre-PDT BCVA and greatest linear dimension (GLD) did not differ between the two groups. The mean BCVA (logMAR) was significantly improved at 6 months post-initial PDT (post-PDT) in the PCV group (-0.11, P = 0.0091). However, at 60 months post-PDT, the mean BCVA was significantly worse than baseline in the tAMD (+0.21, P = 0.0035) and PCV (+0.21, P = 0.0076) groups. Pre-PDT BCVA, age, and GLD were the factors significantly associated with the BCVA at 60 months post-PDT. Although the frequency of recurrence did not significantly differ between the two phenotype groups, the mean recurrence period was significantly longer in the PCV group than in the tAMD group (15.7 vs. 8.6 months, P = 0.0020).

CONCLUSIONS: PDT may not have benefits for visual acuity in cases of tAMD and PCV over 5 years of follow-up.

PMID: 23508554 [PubMed - as supplied by publisher]

Retina. 2013 Mar 15. [Epub ahead of print]

PRECURSORS OF TYPE 3 NEOVASCULARIZATION: A Multimodal Imaging Analysis.

Querques G, Querques L, Forte R, Massamba N, Blanco R, Souied EH.

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PURPOSE: To study the advent of exudative age-related macular degeneration in uninvolved fellow eyes of patients with unilateral Type 3 neovascularization and to investigate the precursors at the site of lesion development.

METHODS: We studied 37 consecutive patients with the diagnosis of unilateral Type 3 neovascularization, for the advent of exudative age-related macular degeneration in uninvolved fellow eyes (study eyes). Looking for the precursors of Type 3 neovascularization, we reviewed the multimodal imaging (fundus autofluorescence, fluorescein angiography, indocyanine green angiography, and spectral-domain optical coherence tomography) in the study eyes and interpreted the changes over time at the site of lesion development.

RESULTS: Of the 37 patients, 12 (32%) developed exudative age-related macular degeneration in the study eye, after a mean of 19.6 ± 9.5 months (range, 9-36 months) from the diagnosis of Type 3 neovascularization in the first involved eye (baseline). All these patients (12 of 12 eyes; 100%) developed Type 3 neovascularization in the study eye. Retrospective analysis of the precursors of these lesions revealed, at baseline, a focal hyperautofluorescence (fundus autofluorescence) that turned to focal hypoautofluorescence over time. In all eyes, a focal hyperfluorescence (fluorescein angiography and indocyanine green angiography) appeared over time at the site of Type 3 neovascularization development. The corresponding spectral-domain optical coherence tomography showed a localized retinal pigment epithelial (RPE) elevation characterized by a focal disruption of the RPE and photoreceptors and by the overlying outer plexiform layer that progressively took contact with the RPE. Based on these findings, it seems that a small, localized RPE elevation might be the lesion before the development of Type 3 neovascularization. This precursor lesion progresses over time to focal atrophy of RPE and photoreceptor.

CONCLUSION: Type 3 neovascularization presents a predictable symmetry and bilaterality. Identification of the precursors of Type 3 neovascularization looks particularly useful for clinicians to detect the earliest changes in the vasogenic process in the fellow eye.

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Retina. 2013 Mar 15. [Epub ahead of print]

SAFETY TESTING OF EPIMACULAR BRACHYTHERAPY WITH MICROPERIMETRY AND INDOCYANINE GREEN ANGIOGRAPHY: 12-Month Results.

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PURPOSE: To determine if epimacular brachytherapy is associated with reduced retinal sensitivity or choroidal nonperfusion.

METHODS: A prospective intervention case series of 12 participants with neovascular age-related macular degeneration requiring frequent ranibizumab underwent vitrectomy and epimacular brachytherapy. The Strontium 90/Yttrium 90 source delivered a single 24-Gy dose at the center of the treatment zone. The dose attenuated with increasing distance from the source. Microperimetry and indocyanine green angiography were performed at baseline and 12 months. The main outcome measures were mean sensitivity and choroidal nonperfusion. A linear mixed model was used to assess the association between the dose of radiation and the change in mean sensitivity.

RESULTS: Mean visual acuity remained within 1 letter of baseline at 12 months (-0.33 ± 13.2 letters). There was no statistically significant change in mean sensitivity within the neovascular age-related macular degeneration lesion area (gain of 0.94 ± 3.25 dB; P = 0.339) or in neighboring unaffected retina (0.66 ± 4.14 dB; P = 0.594), defined using fluorescein angiography. Within the lesion area, mean sensitivity improved by an average of 0.23 ± 0.16 dB (P = 0.006) for every additional gray of radiation received. Indocyanine green angiography failed to demonstrate any choroidal nonperfusion or radiation damage at 12 months after the treatment.

CONCLUSION: Stable retinal sensitivity in areas not manifestly affected by neovascular age-related macular degeneration suggests that epimacular brachytherapy does not damage retinal function. The presence of a dose response suggests that the positive effect of epimacular brachytherapy relates more to beta irradiation than vitrectomy.

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Vision Res. 2013 Mar 15. pii: S0042-6989(13)00043-6. doi: 10.1016/j.visres.2013.02.015. [Epub ahead of print]

Measuring Reading Performance.

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Abstract: Despite significant changes in the treatment of common eye conditions like cataract and age-related macular degeneration, reading difficulty remains the most common complaint of patients referred for low vision services. Clinical reading tests have been widely used since Jaeger introduced his test types in 1854. A brief review of the major developments in clinical reading tests is provided, followed by a discussion of some of the main controversies in clinical reading assessment. Data for the Salisbury Eye Evaluation (SEE) study demonstrate that standardised clinical reading tests are highly predictive of reading performance under natural, real world conditions, and that discrepancies between self-reported reading ability and measured reading performance may be indicative of people who are at a pre-clinical stage of disability, but are at risk for progression to clinical disability. If measured reading performance is to continue to increase in importance as a clinical outcome measure, there must be agreement on what should be measured (e.g. speed or comprehension) and how it should be measured (e.g. reading silently or aloud). Perhaps most important, the methods for assessing reading performance and the algorithms for scoring reading tests need to be optimised so that the reliability and responsiveness of reading tests can be improved.

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Pathogenesis

PLoS One. 2013;8(3):e58096. doi: 10.1371/journal.pone.0058096. Epub 2013 Mar 8.

An angiogenic role for adrenomedullin in choroidal neovascularization.

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PURPOSE: Adrenomedullin (ADM) has been shown to take part in physiological and pathological angiogenesis. The purpose of this study was to investigate whether ADM signaling is involved in choroidal neovascularization (CNV) using a mouse model.

METHODS AND RESULTS: CNV was induced by laser photocoagulation in 8-week-old C57BL/6 mice. ADM mRNA expression significantly increased following treatment, peaking 4 days thereafter. The expression of ADM receptor (ADM-R) components (CRLR, RAMP2 and RAMP 3) was higher in CD31(+)CD45(-) endothelial cells (ECs) than CD31(-)CD45(-) non-ECs. Inflammatory stimulation upregulated the expression of ADM not only in cell lines but also in cells in primary cultures of the choroid/retinal pigment epithelium complex. Supernatants from TNFα-treated macrophage cell lines potentiated the proliferation of ECs and this was partially suppressed by an ADM antagonist, ADM (22-52). Intravitreous injection of ADM (22-52) or ADM neutralizing monoclonal antibody (mAb) after laser treatment significantly reduced the size of CNV compared with vehicle-treated controls ($p<0.01$).

CONCLUSIONS: ADM signaling is involved in laser-induced CNV formation, because both an ADM antagonist and ADM mAb significantly inhibited it. Suppression of ADM signaling might be a valuable alternative treatment for CNV associated with age-related macular degeneration.

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J Ophthalmic Vis Res. 2012 Oct;7(4):316-27.

The cell-matrix interface: a possible target for treating retinal vascular related pathologies.

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Abstract: Retinal vasculature related pathologies account for a large proportion of global blindness. Choroidal neovascularization accompanying age-related macular degeneration is the largest cause of blindness in people over the age of 65 years, proliferative diabetic retinopathy is the main cause of acquired blindness in working adults, and retinopathy of prematurity (ROP) is the leading cause of acquired blindness in children. Given the great success in treating the first category of these conditions with anti-vascular endothelial growth factor (anti-VEGF) therapy, there is understandably considerable interest to employ this strategy to other retinal vascular disorders. Anti-VEGF therapy may not be the optimal course of action, as it may compromise neuronal survival; this is of particular concern when treating ROP where retinal neurogenesis is still not complete. Moreover, retinal neovascularization is preceded by alterations in the vascular wall extracellular matrix with concomitant reduction in mural cell adhesion. This produces vascular instability followed by the pathobiologic process of neovascularization. Thus, stabilizing mural cell-matrix interactions would be a prudent alternative for controlling retinal vascular pathologies. In this review, we will summarize the development of retinal angiogenesis focusing on the role of cell-matrix interaction in each step of the process. Our goal is to identify potential targets for regulating and maintaining normal vascular development and function.

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Invest Ophthalmol Vis Sci. 2013 Mar 21. pii: iovs.12-11020v1. doi: 10.1167/iovs.12-11020. [Epub ahead of print]

All-trans-Retinal Sensitizes Human RPE Cells to Alternative Complement Pathway-Induced Cell Death.

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PURPOSE: Retinal pigment epithelial (RPE) cell death occurs early in the pathogenesis of age-related macular degeneration (AMD) and Stargardt's disease. Emerging evidence suggests that all-trans-retinal (atRal) and alternative complement pathway (AP) activation contribute to RPE cell death in both of these retinal disorders. The aim of this study was to investigate the combined effect of atRal and AP activation on RPE cell viability.

METHODS: RPE cells were treated with atRal and then incubated with a complement-fixing antibody followed by stimulation with C1q-depleted serum to activate AP. Cell viability was assessed by tetrazolium salt and lactate dehydrogenase release assays. Changes in cell surface CD46 and CD59 expression were assessed by flow cytometry. Cells were pre-treated with the antioxidant resveratrol and C1q-depleted serum was incubated with an anti-C5 antibody prior to initiating AP attack to determine the protective effects of antioxidant therapy and complement inhibition, respectively.

RESULTS: Both atRal and AP activation independently caused RPE cell death. When AP attack was initiated following atRal treatment, a synergistic increase in cell death was observed. Following 24-hour atRal treatment, CD46 and CD59 expression decreased, corresponding temporally to increased susceptibility to AP attack. Resveratrol and the anti-C5 antibody both protected against AP-induced cell death following atRal exposure and were most effective when used in combination.

CONCLUSIONS: atRal sensitizes RPE cells to AP attack, which may be mediated in part by atRal-induced down-regulation of CD46 and CD59. Despite increased susceptibility to AP attack following exposure to atRal, resveratrol and anti-C5 antibody effectively prevent AP-mediated cell death.

PMID: 23518773 [PubMed - as supplied by publisher]

Epidemiology

Ophthalmic Epidemiol. 2013 Apr;20(2):82-8. doi: 10.3109/09286586.2012.757626.

The Association between Diagnosed Glaucoma and Cataract and Cognitive Performance in very old People: Cross-sectional Findings from the Newcastle 85+ Study.

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Purpose: Common age-related eye diseases including glaucoma, cataract and age-related macular degeneration (AMD) have been proposed to be associated with dementia. Few studies have examined the relationship between cognition and cataract or glaucoma. We explored the association between cognition and cataract and glaucoma diagnoses in community-dwelling 85-year-olds.

Methods: Cross-sectional analysis of data from the Newcastle 85+ Study. Diagnoses of eye disease were extracted from family practice records. Cognitive performance was assessed by the standardized mini-mental state examination (sMMSE) and the sMMSE-blind (MMblind). Relationships between glaucoma diagnosis or cataract diagnosis and lower cognition were examined using ordinal logistic regression.

Results: Complete data were available for 839 participants. Of these, 36.0% (302/839) had recorded previous cataract surgery, 11.2% (94/839) untreated cataract and 7.9% (66/839) diagnosed glaucoma. Glau-

coma diagnosis was associated with lower sMMSE results (odds ratio [OR] 1.76, 95% confidence interval [CI] 1.05-2.95); but not lower MMblind (OR 1.17, 95% CI 0.65-2.12). When compared to no cataract, cataract diagnosis (treated and untreated combined) was associated with higher sMMSE (OR 0.55, 95% CI 0.38-0.79) and MMblind (OR 0.51, 95% CI 0.34-0.76). Previously treated cataract was associated with higher sMMSE (OR 0.72, 95% CI 0.59-0.88) and MMblind (OR 0.68, 95% CI 0.55-0.85). Untreated cataract was not significantly associated with sMMSE (OR 0.65, 95% CI 0.36-1.19) or MMblind (OR 0.73, 95% CI 0.39-1.36).

Conclusions: This large epidemiological study of 85-year-olds found that lower sMMSE but not MMblind was associated with glaucoma diagnosis, suggesting the association may be driven by poor vision. Cataract diagnosis was associated with higher sMMSE and MMblind. Reasons for this observation are unclear but may relate to enhanced help-seeking behavior in people with diagnosed cataract.

PMID: 23510311 [PubMed - in process]

Ophthalmic Epidemiol. 2013 Apr;20(2):71-81. doi: 10.3109/09286586.2012.759598.

Ten-Year Incidence Rates of Age-Related Cataract in the Age-Related Eye Disease Study (AREDS): AREDS Report No. 33.

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Purpose: To investigate the long-term incidence of age-related cataract and cataract surgery in the Age-Related Eye Disease Study (AREDS) cohort.

Methods: Baseline and annual lens photographs of participants, aged 55-80 years, were graded centrally for nuclear, cortical, and posterior subcapsular (PSC) lens opacities using the AREDS System for Classifying Cataracts. Progression from a baseline status of no or mild lens opacity to at least moderate severity was analyzed and cumulative incidence estimated rates were calculated for each lens opacity type and cataract surgery stratified by age, sex, race, age-related macular degeneration category, multivitamin (Centrum) use and history of diabetes.

Results: The ten-year cumulative incidence was 43.6% for any cataract, 23.1% for nuclear cataract, 22.0% for cortical cataract, 13.1% for PSC cataract, and 26.8% for cataract surgery. The 5- and 10-year incidence rates of all cataract types and cataract surgery were significantly higher with increasing age. Females had a higher incidence of any, nuclear and cortical cataract and cataract surgery ($p = 0.02$-0.05). Incidence of cortical cataract was higher in non-white participants ($p = 0.001$).

Conclusions: These results are largely consistent with the results of previous observational studies. Long-term incidence rates of type-specific cataract can be useful in designing clinical studies of age-related cataract.

PMID: 23510310 [PubMed - in process]

Ophthalmic Surg Lasers Imaging Retina. 2013 Mar 1;44(2):133-9. doi: 10.3928/23258160-20130313-06.

The importance of keeping a broad differential in retina clinic: the spectrum of ophthalmic disease seen by retina specialists in a tertiary outpatient clinic setting.

Fijalkowski N, Pershing S, Moshfeghi DM.

BACKGROUND AND OBJECTIVE: To describe the new patient population referred to retina specialists at

tertiary ophthalmic academic centers in the United States.

STUDY DESIGN AND METHODS: Retrospective chart review of all new patients seen by retina specialists at Stanford University from 2008 to 2011.

RESULTS: Retina specialists saw 7,197 new patients during the study period, with a mean age of 52.2 ± 25.6 years (range: 0 to 108 years). Younger patients (0 to 10 years) were more likely male (P < .001) while older patients were more likely female (P < .01 for 61 to 70, 81+ years). The most common diagnoses were diabetic eye disease (17.0%), retinopathy of prematurity (9.9%) and age-related macular degeneration (9.5%).

CONCLUSION: Retina specialists treat patients of all ages, and the most common diagnoses vary with age and gender. Patients present to retinal clinic with a vast spectrum of disease from various ophthalmic and systemic etiologies; therefore, it is important to maintain a broad differential diagnosis.[Ophthalmic Surg Lasers Imaging Retina. 2013;44:133-139].

PMID: 23510039 [PubMed - in process]

Genetics

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Targeting inflammation in emerging therapies for genetic retinal disease.

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Abstract: Genetic retinal diseases such as age-related macular degeneration and monogenic diseases such as retinitis pigmentosa account for some of the commonest causes of blindness in the developed world. Diverse genetic abnormalities and environmental causes have been implicated in triggering multiple pathological mechanisms such as oxidative stress, lipofuscin deposits, neovascularisation, and programmed cell death. In recent years, inflammation has also been highlighted although whether inflammatory mediators play a central role in pathogenesis or a more minor secondary role has yet to be established. Despite this, numerous interventional studies, particularly targeting the complement system, are underway with the promise of novel therapeutic strategies for these important blinding conditions.

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Deciphering mutant ELOVL4 activity in autosomal-dominant Stargardt macular dystrophy.

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Abstract: Autosomal-dominant Stargardt-like macular dystrophy [Stargardt3 (STGD3)] results from single allelic mutations in the elongation of very-long-chain fatty acids-like 4 (ELOVL4), whereas recessive mutations lead to skin and brain dysfunction. ELOVL4 protein localizes to the endoplasmic reticulum, where it mediates the condensation reaction catalyzing the formation of very-long-chain (VLC) (C-28 to C-40) fatty acids, saturated and polyunsaturated (PUFA). The defective gene product is truncated at the C terminus, leading to mislocalization and aggregation in other organelles. We hypothesized that the STGD3 truncated mutant may generate mislocalized, and therefore toxic, keto intermediates of fatty acid elongation, thereby

contributing to the disease process. Using cell-based and cell-free microsome assays, we found that the truncated protein lacked innate condensation activity. Coexpression of different forms of wild-type and mutant ELOVL4 revealed a large dominant-negative effect of mutant protein on ELOVL4 localization and enzymatic activity, resulting in reduced VLC-PUFA synthesis. The reduction in VLC-PUFA levels in STGD3 and age-related macular degeneration may be a contributing factor to their retinal pathology.

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Am J Ophthalmol. 2013 Mar 13. pii: S0002-9394(13)00075-5. doi: 10.1016/j.ajo.2013.01.019. [Epub ahead of print]

Association of Complement Factor H Tyrosine 402 Histidine Genotype with Posterior Involvement in Sarcoid-Related Uveitis.

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PURPOSE: To determine whether the complement factor H (CFH) tyrosine 402 histidine (Y402H) variant, recently shown to be associated with age-related macular degeneration (AMD) and multifocal choroiditis, is associated with specific ocular sarcoidosis clinical phenotypes in black and white persons.

DESIGN: Case-control study.

METHODS: The CFH Y402H polymorphism (rs1061170) was genotyped in 41 subjects with ocular sarcoidosis and 393 control subjects. Allele frequencies in the ocular sarcoidosis cases were compared with controls using chi-square score tests. Genotypic model-based (dominant, recessive, and additive) associations of the rs1061170 allele were tested using multivariate logistic regression. Bayesian information criteria were used to formalize model selection. Genotypes were correlated with disease characteristics and severity of ocular inflammation.

RESULTS: The C allele (rs1061170) was found in 35% of controls, but occurred with a significantly higher frequency (48.7%) in ocular sarcoidosis cases (odds ratio, 1.72; 95% confidence interval, 1.09 to 2.78; P = .018). Logistic regression demonstrated an association between rs1061170 and ocular sarcoidosis in 2 of 3 genetic models (additive, P = .0078; recessive, P = .0018). Posterior uveitis and panuveitis were overrepresented significantly in cases with the homozygous variant genotype (CC, 91%; P = .047). The population-attributable risk related to this CFH risk variant was 20%.

CONCLUSIONS: The Y402H polymorphism of CFH seems to be associated with ocular sarcoidosis in black and white persons. Carriage of the CFH Y402H polymorphism in both alleles is associated with an increased risk for posterior uveitis and panuveitis presentation. The prognostic importance of this genotype will require prolonged follow-up studies.

PMID: 23497844 [PubMed - as supplied by publisher]

Diet

JAMA Ophthalmol. 2013 Mar 21:1-9. doi: 10.1001/jamaophthalmol.2013.2851. [Epub ahead of print]

Macular Xanthophylls and ω-3 Long-Chain Polyunsaturated Fatty Acids in Age-Related Macular Degeneration: A Randomized Trial.

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IMPORTANCE: It has been shown that the functionality of the macula lutea depends on the nutritional uptake of lutein and zeaxanthin and that it is inversely associated with the risk of age-related macular degen-

eration (AMD). Additionally, ω-3 long-chain polyunsaturated fatty acids (LC-PUFAs) may also be protective.

OBJECTIVE: To investigate the effect of a 12-month intervention with macular xanthophylls and ω-3 LC-PUFAs on xanthophylls and fatty acids in plasma, antioxidant capacity, and optical density of the macular pigment of patients with nonexudative AMD. DESIGN The LUTEGA study was a randomized, double-blind, placebo-controlled, parallel clinical trial that was conducted for 12 months.

SETTING: University Eye Hospital and Institute of Nutrition, Friedrich Schiller University Jena, Germany. PARTICIPANTS A total of 172 individuals with nonexudative AMD.

INTERVENTION: Individuals were enrolled and randomly divided as follows: placebo group, group 1 (a capsule containing 10 mg of lutein, 1 mg of zeaxanthin, 100 mg of docosahexaenoic acid, and 30 mg of eicosapentaenoic acid administered each day), and group 2 (same substances but twice the dose used in group 1). One hundred forty-five participants completed the study successfully.

MAIN OUTCOME MEASURES: Plasma xanthophyll concentrations and fatty acid profiles, optical density of the macular pigment, and antioxidant capacity in plasma (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid [Trolox] equivalent antioxidant capacity and photochemiluminescence).

RESULTS: The concentrations of the administered carotenoids in plasma as well as the optical density of the macular pigment increased significantly in the groups randomized to receive supplementary macular xanthophylls and ω-3 LC-PUFAs after 1 month of intervention and remained at this level through the end of the study. Use of the double dose resulted in a beneficial alteration of the fatty acid profile in the plasma of patients with AMD in comparison with the dose in group 1. The lipophilic antioxidant capacity in plasma was significantly elevated with the intervention.

CONCLUSIONS AND RELEVANCE: A supplement containing a fixed combination of lutein, zeaxanthin, and ω-3 LC-PUFAs during 12 months significantly improved plasma antioxidant capacity, circulating macular xanthophyll levels, and the optical density of the macular pigment.

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