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Drug treatment

Ophthalmology. 2016 Feb 27. [Epub ahead of print]

Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema: Two-Year Results from a Comparative Effectiveness Randomized Clinical Trial.

Wells JA, Glassman AR, Ayala AR, Jampol LM, Bressler NM, Bressler SB, Brucker AJ, Ferris FL, Hampton GR, Jhaveri C, Melia M, Beck RW; Diabetic Retinopathy Clinical Research Network.

PURPOSE: To provide 2-year results comparing anti-vascular endothelial growth factor (VEGF) agents for center-involved diabetic macular edema (DME) using a standardized follow-up and retreatment regimen.

DESIGN: Randomized clinical trial.

PARTICIPANTS: Six hundred sixty participants with visual acuity (VA) impairment from DME.

METHODS: Randomization to 2.0-mg aflibercept, 1.25-mg repackaged (compounded) bevacizumab, or 0.3-mg ranibizumab intravitreal injections performed up to monthly using a protocol-specific follow-up and retreatment regimen. Focal/grid laser photocoagulation was added after 6 months if DME persisted. Visits occurred every 4 weeks during year 1 and were extended up to every 4 months thereafter when VA and macular thickness were stable.

MAIN OUTCOME MEASURES: Change in VA, adverse events, and retreatment frequency.

RESULTS: Median numbers of injections were 5, 6, and 6 in year 2 and 15, 16, and 15 over 2 years in the aflibercept, bevacizumab, and ranibizumab groups, respectively (global $P = 0.08$). Focal/grid laser photocoagulation was administered in 41%, 64%, and 52%, respectively (aflibercept vs. bevacizumab, $P < 0.001$; aflibercept vs. ranibizumab, $P = 0.04$; bevacizumab vs. ranibizumab, $P = 0.01$). At 2 years, mean VA improved by 12.8, 10.0, and 12.3 letters, respectively. Treatment group differences varied by baseline VA ($P = 0.02$ for interaction). With worse baseline VA (20/50 to 20/320), mean improvement was 18.1, 13.3, and 16.1 letters, respectively (aflibercept vs. bevacizumab, $P = 0.02$; aflibercept vs. ranibizumab, $P = 0.18$; ranibizumab vs. bevacizumab, $P = 0.18$). With better baseline VA (20/32 to 20/40), mean improvement was 7.8, 6.8, and 8.6 letters, respectively ($P > 0.10$, for pairwise comparisons). Anti-Platelet Trialists' Collaboration (APT) events occurred in 5% with aflibercept, 8% with bevacizumab, and 12% with ranibizumab (global $P = 0.047$; aflibercept vs. bevacizumab, $P = 0.34$; aflibercept vs. ranibizumab, $P = 0.047$; ranibizumab vs. bevacizumab, $P = 0.20$; global $P = 0.09$ adjusted for potential confounders).

CONCLUSIONS: All 3 anti-VEGF groups showed VA improvement from baseline to 2 years with a decreased number of injections in year 2. Visual acuity outcomes were similar for eyes with better baseline VA. Among eyes with worse baseline VA, aflibercept had superior 2-year VA outcomes compared with bevacizumab, but superiority of aflibercept over ranibizumab, noted at 1 year, was no longer identified. Higher APT event rates with ranibizumab over 2 years warrants continued evaluation in future trials.

PMID: 26935357 [PubMed - as supplied by publisher]

Ophthalmologica. 2016 Mar 1. [Epub ahead of print]

The Effectiveness of Intravitreal Ranibizumab in Patients with Diabetic Macular Edema Who Have Failed to Respond to Intravitreal Bevacizumab.

Ehrlich R, Dan I, Deitch I, Axer-Siegel R, Mimouni K.

PURPOSE: To investigate the response to intravitreal ranibizumab after failure of intravitreal bevacizumab in patients with diabetic macular edema (DME).

METHODS: Demographics, visual acuity (VA), central macular thickness (CMT), and HbA1C were retrospectively collected from DME patients treated with second-line intravitreal ranibizumab at a tertiary hospital in 2012-2013 and followed for at least 3 months.

RESULTS: Twenty-two patients (26 eyes) were included in the study, with a mean ($\pm$ SD) age of 66 ± 8.1 years and followed for an average of 28.36 months. The mean number of intravitreal bevacizumab injections was 7.3 ± 2.8 , and of intravitreal ranibizumab injections 5.11 ± 2.4 . After 3 ranibizumab injections, 57% of eyes showed improvement in VA. The change in VA was statistically significant ($p = 0.044$) in those eyes where the pretreatment acuity for the second-line therapy was $<20/40$ (logMAR 0.3). CMT decreased from 435.95 ± 83.28 to $373.69 \pm 44.39 \mu\text{m}$ ($p = 0.01$). The number of ranibizumab injections was significantly correlated with the change in CMT ($p = 0.037$).

CONCLUSION: Intravitreal treatment with ranibizumab can be efficacious in eyes with DME that have failed to respond to bevacizumab.

PMID: 26926483 [PubMed - as supplied by publisher]

J Ocul Pharmacol Ther. 2016 Mar 3. [Epub ahead of print]

A Prospective Masked Clinical Assessment of Inflammation After Intravitreal Injection of Ranibizumab or Aflibercept.

Khanani AM, Cohen GL, Zawadzki R.

PURPOSE: To compare anterior chamber and vitreous inflammation after intravitreal injection of ranibizumab or aflibercept.

METHODS: This was a prospective, open label, nonrandomized phase 4 clinical study. One hundred patients with choroidal neovascularization due to age-related macular degeneration received intravitreal aflibercept ($N = 53$) or ranibizumab ($N = 47$). Medication use was balanced by gender, injected eye, and lens status (phakic vs. pseudophakic). An examiner masked to medication graded anterior chamber and vitreous inflammation 1-2 and 5-7 days after injection according to the Standardization of Uveitis Nomenclature grading scheme.

RESULTS: Mean patient age was 78.6 years. Maximum anterior chamber reaction of 0.5+ was seen at the first postinjection examination in 2% of eyes receiving ranibizumab and in 19% of eyes receiving aflibercept (Fisher's exact test 2 sided, $P = 0.0091$); vitreous reaction was minimal and infrequent in both groups and the difference was not statistically significant. At 5-7 days after injection, 1 patient treated with aflibercept had residual anterior chamber inflammation of 0.5+ and no patient treated with ranibizumab had residual inflammation.

CONCLUSION: Aflibercept may be associated with more anterior chamber inflammation than ranibizumab, although mild and transient. This should not be mistaken for endophthalmitis.

PMID: 26938579 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2016 Feb 17;10:313-9. eCollection 2016.

Three-year follow-up of ranibizumab treatment of wet age-related macular degeneration: influence of baseline visual acuity and injection frequency on visual outcomes.

Razi F, Haq A, Tonne P, Logendran M.

PURPOSE: To determine the effect of ranibizumab on visual acuity (VA) following a 3-year treatment period for patients diagnosed with wet age-related macular degeneration. To establish whether baseline VA and injection frequency influence visual outcomes.

PATIENTS AND METHODS: Retrospective review of 70 patients (76 eyes) treated with 0.5 mg intravitreal ranibizumab for 3 consecutive months, and pro re nata thereafter (three + pro re nata protocol), over a 3-year period. VA was measured using Early Treatment Diabetic Retinopathy Study (ETDRS) charts at baseline, 12, 24, and 36 months. The number of injections administered at the end of years 1, 2, and 3 were also recorded. Eyes were stratified according to baseline VA, as well as the number of injections administered at the end of year 1. Linear regression analysis determined the relationship between VA and both baseline VA and injection frequency. $P < 0.05$ was considered statistically significant.

RESULTS: At 36 months, VA improved by a mean of 5.3 ETDRS letters ($P = 0.002$), with 29% of eyes ($n = 22$) demonstrating a clinically significant improvement in VA (gain of ≥ 15 ETDRS letters). Improvements in VA from baseline to 36 months were inversely proportional to the baseline VA ($R = 0.414$, $P < 0.001$). A positive correlation was observed between injection frequency and change in VA from baseline to 36 months ($R = 0.244$, $P = 0.036$).

CONCLUSION: Mean improvement in VA is inversely proportional to baseline VA, and directly proportional to injection frequency.

PMID: 26937168 [PubMed]

Am J Ophthalmol. 2016 Mar 1. [Epub ahead of print]

Post-injection endophthalmitis rates and characteristics following intravitreal bevacizumab, ranibizumab and aflibercept.

Rayess N, Rahimy E, Storey P, Shah CP, Wolfe JD, Chen E, DeCroos FC, Garg SJ, Hsu J.

PURPOSE: To compare the incidence and clinical outcomes of endophthalmitis following intravitreal injections of bevacizumab, ranibizumab and aflibercept.

DESIGN: Multicenter, retrospective cohort study.

METHODS: All included patients had received intravitreal injections of bevacizumab, ranibizumab or aflibercept between January 1, 2009 and September 30, 2013 at 5 retina practices. Billing records were used to identify the total number of anti-vascular endothelial growth factors (VEGF) injections administered. Patients who developed endophthalmitis were ascertained from endophthalmitis logs and billing records. Chart review of these patients was performed to confirm that the endophthalmitis was related to the antecedent anti-VEGF injection. Visual outcomes, causative organisms and clinical course were also recorded.

RESULTS: A total of 503,890 anti-VEGF injections were included, from which 183 cases of presumed endophthalmitis were identified. The rate of endophthalmitis for bevacizumab was 0.039% (60/153,812), which was similar to ranibizumab 0.035% (109/309,722; $P = 0.522$) and aflibercept 0.035% (14/40,356; $P = 0.693$). Similarly, there was no difference in the rates between ranibizumab and aflibercept ($P = 0.960$). The culture positive rate of the vitreous/aqueous tap was 38% for both bevacizumab and ranibizumab and was 43% for aflibercept. Furthermore, visual acuity remained decreased at 3 months follow-up for bevacizumab ($P = 0.005$), ranibizumab ($P < 0.001$) and aflibercept ($P = 0.07$) compared to vision at causative injection.

CONCLUSIONS: Endophthalmitis following intravitreal bevacizumab, ranibizumab and aflibercept injection appears to occur at similar rates and have comparable visual outcomes. This study suggests that the choice of anti-VEGF agent should be primarily based on efficacy and patient response rather than concern for risk of infection.

PMID: 26944277 [PubMed - as supplied by publisher]

BMJ. 2016 Feb 28;352:i1196.

Aflibercept is better drug for diabetic macular oedema, study finds.

Wise J.

PMID: 26929279 [PubMed - in process]

Ophthalmology. 2016 Feb 26. [Epub ahead of print]

Treatment Patterns and Health Care Costs for Age-Related Macular Degeneration in Japan: An Analysis of National Insurance Claims Data.

Kume A, Ohshiro T, Sakurada Y, Kikushima W, Yoneyama S, Kashiwagi K.

PURPOSE: To investigate changes in the proportion of patients with age-related macular degeneration (AMD) visiting hospitals and to investigate factors associated with AMD, treatments, and medical expenses, as well as the outlook for AMD in Japan using a large health insurance database.

DESIGN: Analysis of national insurance claims data.

PARTICIPANTS: People 40 years of age or older who were registered in the Japan Medical Data Center database.

METHODS: Patients with AMD were identified from 2005 through 2013 based on International Classification of Diseases, 10th revision, diagnosis codes. Changes in patient proportions, treatment procedures, and medical expenses were investigated during the study period. The data for each year were compared after adjustment based on the 2010 Japanese population annual census. The outlook for patients with AMD was predicted based on the combination of data in 2013 and an official future population prediction report.

MAIN OUTCOME MEASURES: Changes in treatment patterns and health care costs in Japan.

RESULTS: A total of 3 401 299 participants were included in the analysis, and 3058 AMD patients were identified over the 9-year period. The proportion of patients with AMD increased significantly from 0.084% (95% confidence interval, 0.050%-0.119%) in 2005 to 0.26% (95% confidence interval, 0.24%-0.29%) in 2013 ($P = 0.0001$, Pearson correlation coefficient test). There were significantly more men than women (odds ratio, 1.25; 95% confidence interval, 1.14-1.37), and the proportion of patients with AMD increased rapidly with age. Photodynamic therapy was replaced by anti-vascular endothelial growth factor (VEGF) therapy as the predominant therapy from 2009 onward. Medical expenses per 10 000 persons increased from \$1530 to \$137 000 over the 9-year period. The proportion of AMD patients is predicted to increase in the future and will reach a maximum of 223 000 in 2035.

CONCLUSIONS: The proportion of AMD patients visiting hospitals, medical expenses, and the frequency of anti-VEGF therapy increased significantly over the 9-year period. These increasing trends are predicted to continue in Japan.

PMID: 26927204 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Am J Ophthalmol. 2016 Feb 29. [Epub ahead of print]

Relating retinal morphology and function in aging and early to intermediate age-related macular degeneration subjects.

Sevilla MB, McGwin G Jr, Lad EM, Clark M, Yuan EL, Farsiu S, Curcio CA, Owsley C, Toth CA.

PURPOSE: To evaluate relationships between age-related macular degeneration (AMD) morphology on spectral domain optical coherence tomography (SDOCT) and visual function.

DESIGN: Cross-sectional, observational.

METHODS: From the Alabama Study on Early AMD baseline visit, visual acuity, cone-mediated sensitivity (Humphrey Field Analyzer, Carl Zeiss Meditec, Dublin, CA), rod-mediated dark adaptation (AdaptDx, MacuLogix, Hummelstown, PA), and SDOCT (Spectralis, Heidelberg Engineering, Germany) were obtained in one eye per subject with No Apparent Retinal Aging (N=15), Normal Aging (N=15), Early AMD (N=15), and Intermediate (N=46) AMD. The volumes of retinal pigment epithelium (RPE)-drusen-complex, RPE-drusen-complex abnormal thinning, RPE-drusen-complex abnormal thickening and inner and outer retina were calculated in specified regions using semi-automated SDOCT segmentation.

RESULTS: Better cone-mediated sensitivity was associated with greater RPE-drusen-complex volume ($r=0.34$, $p<0.001$) and less RPE-drusen-complex abnormal thinning volume ($r=-0.31$, $p=0.003$). Longer rod-mediated dark adaptation time, the duration for rod-mediated sensitivity to recover from photo-bleach exposure, correlated with lower RPE-drusen-complex volume ($r=-0.34$, $p=0.005$) and greater RPE-drusen-complex abnormal thinning volume ($r=0.280$, $p=0.023$). In 19 eyes with subretinal drusenoid deposits (SDD) versus 47 eyes without SDD, rod-mediated dark adaptation time was longer (mean $\pm$ SD 13.5 ± 7.0 versus 10.2 ± 3.1 minutes, $p=0.004$), RPE-drusen-complex abnormal thinning volume was greater ($p<0.0001$), and visual acuity and cone sensitivity did not differ.

CONCLUSION: Decreased function relates to structural markers on SDOCT in AMD. Because the RPE-drusen-complex includes the interdigitation of outer segments and RPE apical processes and SDD in eyes with AMD, slower dark adaptation might be related to structural abnormalities of the RPE, the RPE-photoreceptor interface, or both.

PMID: 26940163 [PubMed - as supplied by publisher]

Retina. 2016 Mar 4. [Epub ahead of print]

TISSUE PLASMINOGEN ACTIVATOR FOR SUBFOVEAL HEMORRHAGE DUE TO AGE-RELATED MACULAR DEGENERATION: Comparison of 3 Treatment Modalities.

Fassbender JM, Sherman MP, Barr CC, Schaal S.

PURPOSE: To analyze and compare the effects of three common treatment modalities for a thick subfoveal hemorrhage due to exudative age-related macular degeneration on final visual acuity and the size of the final subretinal scar.

DESIGN: Retrospective case series.

SETTING: Single-site, tertiary referral center.

PATIENTS: Thirty-nine patients with exudative age-related macular degeneration and acute SMH greater than 250 μ m.

INTERVENTION: Patients received vitrectomy with a subretinal tissue plasminogen activator (tPA) injection, pneumatic displacement (PD) with intravitreal tPA, or PD without tPA within 2 weeks of presentation.

MAIN OUTCOME MEASURE: Functional outcome was determined by Snellen visual acuity. Anatomical outcome was determined as the final disciform scar size.

RESULTS: Treatment groups did not differ in age, sex, initial visual acuity, the initial area of the thick subfoveal hemorrhage, follow-up duration, lens status, duration of exudative age-related macular degeneration, previous intravitreal bevacizumab injections, or time from last given injection to the acute thick subfoveal hemorrhage. Final visual acuity improved significantly in both the vitrectomy and subretinal tPA injection group ($P < 0.001$), and the intravitreal tPA injection group ($P = 0.002$) but not with PD alone. Patients treated with subretinal tPA achieved $40\% \pm 54\%$ reduction in final scar area, in contrast to $27\% \pm 35\%$ decrease in patients treated with intravitreal tPA ($P = 0.001$).

CONCLUSION: Treatment with tPA improves the functional and anatomical outcomes in patients with thick subfoveal hemorrhage due to subfoveal choroidal neovascular membrane secondary to exudative age-related macular degeneration and was superior to PD without tPA. Vitrectomy with subretinal tPA injection reduced the final disciform scar compared with PD with or without intravitreal tPA.

PMID: 26945238 [PubMed - as supplied by publisher]

Retina. 2016 Feb 24. [Epub ahead of print]

VISUAL FUNCTION MEASURES IN EARLY AND INTERMEDIATE AGE-RELATED MACULAR DEGENERATION.

Chandramohan A, Stinnett SS, Petrowski JT, Schuman SG, Toth CA, Cousins SW, Lad EM.

PURPOSE: The objectives of this study were to evaluate 1) the feasibility of performing computerized tests of low luminance visual acuity (LLVA), cone-specific contrast (Cone Contrast Test [CCT]), contrast sensitivity, and microperimetry and 2) the test-retest repeatability of these outcomes in dry age-related macular degeneration (AMD).

METHODS: This prospective study enrolled 30 subjects at a single site (8 controls, 8 early AMD, and 12 intermediate AMD). Subjects underwent LLVA, contrast sensitivity, CCT, and microperimetry with eye tracking. Low luminance deficit was defined as best-corrected visual acuity minus LLVA in EDTRS letters. Follow-up testing was administered at approximately 1 month.

RESULTS: There was high test-retest repeatability at one month for all visual function metrics (intraclass correlations >0.7) except log contrast sensitivity (intraclass correlations 0.6). Compared with controls, patients with intermediate AMD showed significant deficits on best-corrected visual acuity, LLVA, low luminance deficit, percent-reduced threshold on microperimetry, and red CCT ($P < 0.05$), but not on contrast sensitivity, green and blue CCT.

CONCLUSION: This pilot study supports the feasibility and reliability of using LLVA, microperimetry, and CCT in early dry AMD. Our data suggest these measures can be used as alternative future clinical trial endpoints. A larger, prospective natural history study of alternative visual function measures in dry AMD is warranted.

PMID: 26925551 [PubMed - as supplied by publisher]

Retin Cases Brief Rep. 2016 Mar 1. [Epub ahead of print]

ATYPICAL MACULOPATHY IN A PATIENT WITH LIGHT CHAIN DEPOSITION DISEASE MIMICKING ADVANCED GEOGRAPHIC ATROPHY.

Crawford C, Oshry LJ, Reichel E.

PURPOSE: To report a previously unreported presentation of advanced geographic atrophy of the macula

mimicking nonneovascular (dry) age-related macular degeneration in a patient with light chain deposition disease.

METHODS: Ocular examination included dilated fundus examination, fundus autofluorescence, full-field electroretinography, and spectral domain optical coherence tomography.

PATIENTS: Single-patient case report.

RESULTS: Dilated fundus examination demonstrated diffuse loss of the retinal pigment epithelium in a geographic atrophy pattern in the macula and drusenlike deposits localized to the outer retina and retinal pigment epithelium. There were no signs of choroidal neovascularization or retinal pigment epithelium detachments. Fundus autofluorescence demonstrated wide areas of retinal pigment epithelium loss. Full-field electroretinography was normal. Spectral domain optical coherence tomography displayed atrophy of the outer retinal layers.

DISCUSSION: This is the first documented case of drusenlike deposits and maculopathy in a patient with light chain deposition disease that mimics advanced geographic atrophy that is typically observed in nonneovascular age-related macular degeneration. Physicians should be aware of the macular changes that can be associated with light chain deposition disease, and patients with light chain deposition disease should be regularly evaluated for associated macular disease. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND), which permits downloading and sharing the work provided it is properly cited. The work cannot be changed in any way or used commercially.

PMID: 26934302 [PubMed - as supplied by publisher]

Optom Vis Sci. 2016 Feb 26. [Epub ahead of print]

A Color Perimetric Test to Evaluate Macular Pigment Density in Age-Related Macular Degeneration.

Demirel S, Ozmert E, Batoglu F, Gedik-Oguz Y.

PURPOSE: To evaluate differences in measurements of macular pigment optical density (MPOD) in patients with dry age-related macular degeneration (AMD) and a group of healthy patients (control group). Short-term repeatability of MPOD measures was also assessed in the control group.

METHODS: This cross-sectional study included 31 eyes from 31 patients with bilateral dry AMD, 21 eyes from 21 cases with dry AMD in the study eye and exudative AMD in the fellow eye. The control group included 17 eyes from 17 healthy patients of similar age and sex. The MPOD values were measured using a commercially available color perimetry technique (CP). Short-term repeatability of MPOD measurements by the CP technique was assessed in 20 eyes of 20 healthy subjects who were measured 3 times on 3 consecutive days.

RESULTS: The mean values for MPOD were 5.59 ± 2.06 dB in cases in which both eyes had dry AMD, 5.25 ± 2.72 dB in cases in which one eye had wet AMD and the studied eye had dry AMD, and 5.97 ± 2.14 dB in the eyes of the healthy control group. The mean value was lower in cases in which the fellow eye had wet AMD; however, no significant difference in MPOD was found between the three groups ($p = 0.659$) or between the group with dry AMD in both eyes and the healthy control group ($p = 0.977$). The intraclass correlation coefficient (ICC) value was 0.664 between day 1 and day 2, and 0.822 between day 2 and day 3.

CONCLUSIONS: Our results do not show a direct relation between MPOD and dry AMD. Color perimetry does not provide acceptable short-term repeatability for measuring MPOD. Learning effects may contribute to the measured test-retest variability. Other studies are needed to determine if CP is suitable for repeated measurements during the long term follow-up with the same patient.

PMID: 26927521 [PubMed - as supplied by publisher]

JAMA Ophthalmol. 2016 Mar 3. [Epub ahead of print]

Spontaneous Closure of a Full-Thickness Macular Hole With Conversion to Exudative Age-Related Macular Degeneration.

Su D, Klufas MA, Hubschman JP.

PMID: 26941005 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2016 Feb 10;10:285-95. eCollection 2016.

Teleophthalmology: improving patient outcomes?

Sreelatha OK, Ramesh SV.

Abstract: Teleophthalmology is gaining importance as an effective eye care delivery modality worldwide. In many developing countries, teleophthalmology is being utilized to provide quality eye care to the underserved urban population and the unserved remote rural population. Over the years, technological innovations have led to improvement in evidence and teleophthalmology has evolved from a research tool to a clinical tool. The majority of the current teleophthalmology services concentrate on patient screening and appropriate referral to experts. Specialty care using teleophthalmology services for the pediatric group includes screening as well as providing timely care for retinopathy of prematurity (ROP). Among geriatric eye diseases, specialty teleophthalmology care is focused toward screening and referral for diabetic retinopathy (DR), glaucoma, age-related macular degeneration (ARMD), and other sight-threatening conditions. Comprehensive vision screening and refractive error services are generally covered as part of most of the teleophthalmology methods. Over the past decades, outcome assessment of health care system includes patients' assessments on their health, care, and services they receive. Outcomes, by and large, remain the ultimate validators of the effectiveness and quality of medical care. Teleophthalmology produces the same desired clinical outcome as the traditional system. Remote portals allow specialists to provide care over a larger region, thereby improving health outcomes and increasing accessibility of specialty care to a larger population. A high satisfaction level and acceptance is reported in the majority of the studies because of increased accessibility and reduced traveling cost and time. Considering the improved quality of patient care and patient satisfaction reported for these telemedicine services, this review explores how teleophthalmology helps to improve patient outcomes.

PMID: 26929592 [PubMed] PMCID: PMC4755429

Pathogenesis

Mol Med Rep. 2016 Feb 22. [Epub ahead of print]

Apr3 accelerates the senescence of human retinal pigment epithelial cells.

Han S, Lu Q, Wang N.

Abstract: Senescence of retinal pigment epithelium (RPE) cells is a major contributor to age-related macular degeneration (AMD). However, the molecular mechanisms underlying RPE dysfunction are not well understood. Apoptosis related protein 3 (Apr3) was originally cloned from HL-60 cells induced by all-trans retinoic acid (ATRA). Preliminary data revealed elevated Apr3 expression in the tissues of aged mice, suggesting that it is involved in the aging process. The present study demonstrated that Apr3 mRNA and protein levels were markedly increased in aged mouse RPE cells. Elevated Apr3 expression was also observed during premature senescence induced by oxidative stress (H₂O₂ and tert-BHP) in ARPE-19 cells. Moreover, Apr3 overexpression promoted cellular senescence in ARPE-19 cells, as characterized by enhanced senescence-associated β -galactosidase activity, reduced cell proliferation and increased expression of the senescence markers p53 and p21. In addition, it was demonstrated that overexpression

of Apr3-N, a truncated counterpart of Apr3, abrogated Apr3-induced phenotypes. It was concluded that Apr3 expression was induced in replicative and premature senescence of RPE cells and its overexpression accelerated senescence of ARPE-19 cells, which provides important insights into the function of Apr3 in senescence-associated diseases.

PMID: 26934949 [PubMed - as supplied by publisher]

Ophthalmic Genet. 2016 Mar 3;1-3. [Epub ahead of print]

Evaluation of C-reactive protein and CC-cytokine ligand 2 polymorphism interaction for age-related macular degeneration.

Jabbarpoor Bonyadi MH, Mohammadian T, Bonyadi M, Soheilian M, Moein H, Yaseri M.

PMID: 26940485 [PubMed - as supplied by publisher]

Sci Rep. 2016 Mar 4;6:22671.

The Silk-protein Sericin Induces Rapid Melanization of Cultured Primary Human Retinal Pigment Epithelial Cells by Activating the NF- κ B Pathway.

Eidet JR, Reppe S, Pasovic L, Olstad OK, Lyberg T, Khan AZ, Fostad IG, Chen DF, Utheim TP.

Abstract: Restoration of the retinal pigment epithelial (RPE) cells to prevent further loss of vision in patients with age-related macular degeneration represents a promising novel treatment modality. Development of RPE transplants, however, requires up to 3 months of cell differentiation. We explored whether the silk protein sericin can induce maturation of primary human retinal pigment epithelial (hRPE) cells. Microarray analysis demonstrated that sericin up-regulated RPE-associated transcripts (RPE65 and CRALBP). Upstream analysis identified the NF- κ B pathway as one of the top sericin-induced regulators. ELISA confirmed that sericin stimulates the main NF- κ B pathway. Increased levels of RPE-associated proteins (RPE65 and the pigment melanin) in the sericin-supplemented cultures were confirmed by western blot, spectrophotometry and transmission electron microscopy. Sericin also increased cell density and reduced cell death following serum starvation in culture. Inclusion of NF- κ B agonists and antagonists in the culture medium showed that activation of the NF- κ B pathway appears to be necessary, but not sufficient, for sericin-induced RPE pigmentation. We conclude that sericin promotes pigmentation of cultured primary hRPE cells by activating the main NF- κ B pathway. Sericin's potential role in culture protocols for rapid differentiation of hRPE cells derived from embryonic or induced pluripotent stem cells should be investigated.

PMID: 26940175 [PubMed - in process]

Transl Vis Sci Technol. 2016 Feb 22;5(1):8. eCollection 2016.

Two Bioactive Molecular Weight Fractions of a Conditioned Medium Enhance RPE Cell Survival on Age-Related Macular Degeneration and Aged Bruch's Membrane.

Sugino IK, Sun Q, Springer C, Cheewatrakoolpong N, Liu T, Li H, Zarbin MA.

PURPOSE: To characterize molecular weight fractions of bovine corneal endothelial cell conditioned medium (CM) supporting retinal pigment epithelium (RPE) cell survival on aged and age-related macular degeneration (AMD) Bruch's membrane.

METHODS: CM was subject to size separation using centrifugal filters. Retentate and filtrate fractions were tested for bioactivity by analyzing RPE survival on submacular Bruch's membrane of aged and AMD donor eyes and behavior on collagen I-coated tissue culture wells. Protein and peptide composition of active

fractions was determined by mass spectrometry.

RESULTS: Two bioactive fractions, 3-kDa filtrate and a 10-50-kDa fraction, were necessary for RPE survival on aged and AMD Bruch's membrane. The 3-kDa filtrate, but not the 10-50-kDa fraction, supported RPE growth on collagen 1-coated tissue culture plates. Mass spectrometry of the 10-50-kDa fraction identified 175 extracellular proteins, including growth factors and extracellular matrix molecules. Transforming growth factor (TGF) β -2 was identified as unique to active CM. Peptides representing 29 unique proteins were identified in the 3-KDa filtrate.

CONCLUSIONS: These results indicate there is a minimum of two bioactive molecules in CM, one found in the 3-kDa filtrate and one in the 10-50-kDa fraction, and that bioactive molecules in both fractions must be present to ensure RPE survival on Bruch's membrane. Mass spectrometry analysis suggested proteins to test in future studies to identify proteins that may contribute to CM bioactivity.

TRANSLATIONAL RELEVANCE: Results of this study are the first steps in development of an adjunct to cell-based therapy to ensure cell transplant survival and functionality in AMD patients.

PMID: 26933521 [PubMed]

Biochem Cell Biol. 2016 Jan 15:1-9. [Epub ahead of print]

TAK1 is involved in the autophagy process in retinal pigment epithelial cells.

Green YA, Ben-Yaakov K, Adir O, Pollack A, Dvashi Z.

Abstract: Autophagy is an evolutionarily conserved mechanism for degrading long-lived or malfunctioning proteins and organelles, such as those resulting from oxidative stress. Several publications have demonstrated the importance of the autophagy process in the pathophysiology of dry age-related macular degeneration (AMD). Still, the mechanism underlying this process and its involvement in dry AMD are not fully characterized. Investigating the autophagy process in retinal pigment epithelial (RPE) cells, we identified transforming growth factor β activated kinase 1 (TAK1) as a key player in the process. We found increased TAK1 phosphorylation in ARPE-19 and D407 cells treated with different inducers of autophagy, such as oxidative stress and rapamycin. Moreover, utilizing TAK1 specific inhibitor prior to oxidative stress or rapamycin treatment, we found significant reduction in LC3A/B-II expression. These results point at the involvement of TAK1 in the regulation of autophagy in RPE cells. This study suggests that aberrant activity of this kinase impairs autophagy and subsequently leads to alterations in the vitality of RPE cells. Proper activity of TAK1 may be essential for efficient autophagy, and crucial for the ability of RPE cells to respond to stress and dispose of damaged organelles, thus preventing or delaying retinal pathologies.

PMID: 26928052 [PubMed - as supplied by publisher]

Exp Eye Res. 2016 Feb 26. [Epub ahead of print]

Axitinib Inhibits Retinal and Choroidal Neovascularization in In vitro and In vivo Models.

Giddabasappa A, Lalwani K, Norberg R, Gukasyan HJ, Paterson D, Schachar RA, Rittenhouse K, Klammer K, Mosyak L, Eswaraka J.

Abstract: Age-related Macular Degeneration (AMD) is the leading cause of visual impairment and blindness in the elderly in developed countries. Neovascular/exudative (wet) AMD is the aggressive form of AMD and can involve choroidal neovascularization and vascular leakage. Anti-vascular endothelial growth factor (anti-VEGF) medications have significantly improved treatment of wet-AMD. However, only approximately 40% of patients obtain full benefit from anti-VEGF therapy and the medications are given by intravitreal injection. Axitinib, a small molecule multi-receptor tyrosine kinase inhibitor used for the treatment of advanced renal cell carcinoma, is taken orally and inhibits VEGF activity by blocking VEGF receptors. Axitinib also has the advantage of blocking platelet derived growth factor (PDGF) receptors which play a role in

neovascularization. Using in vitro human retinal microvascular endothelial cells (HRMVECs), human brain vascular pericytes (HBVRs), 3D co-culture vessel sprout assay, and in vivo laser induced rat choroidal neovascularization (CNV) models, the effect of axitinib on neovascularization was evaluated. Axitinib inhibited neovascularization better than anti-VEGF and/or anti-hPDGF-B mAb in the in vitro models demonstrating that combined inhibition of both VEGF and PDGF pathways may be synergistic in treating wet-AMD. Additionally, axitinib showed good efficacy at a low dose (0.875 mg/day) in laser-induced CNV model in rats. In conclusion our data shows that axitinib, an inhibitor of VEGF and PDGF-B pathways may be useful in ameliorating wet-AMD therapy.

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Signal Transduct Target Ther. 2016;1. Epub 2016 Jan 28.

Intravenous immune globulin suppresses angiogenesis in mice and humans.

Yasuma R, Cicatiello V, Ambati J et al

Abstract: Human intravenous immune globulin (IVIg), a purified IgG fraction composed of ~ 60% IgG1 and obtained from the pooled plasma of thousands of donors, is clinically used for a wide range of diseases. The biological actions of IVIg are incompletely understood and have been attributed both to the polyclonal antibodies therein and also to their IgG (IgG) Fc regions. Recently, we demonstrated that multiple therapeutic human IgG1 antibodies suppress angiogenesis in a target-independent manner via FcγRI, a high-affinity receptor for IgG1. Here we show that IVIg possesses similar anti-angiogenic activity and inhibited blood vessel growth in five different mouse models of prevalent human diseases, namely, neovascular age-related macular degeneration, corneal neovascularization, colorectal cancer, fibrosarcoma and peripheral arterial ischemic disease. Angioinhibition was mediated by the Fc region of IVIg, required FcγRI and had similar potency in transgenic mice expressing human FcγRs. Finally, IVIg therapy administered to humans for the treatment of inflammatory or autoimmune diseases reduced kidney and muscle blood vessel densities. These data place IVIg, an agent approved by the US Food and Drug Administration, as a novel angioinhibitory drug in doses that are currently administered in the clinical setting. In addition, they raise the possibility of an unintended effect of IVIg on blood vessels.

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Front Cell Neurosci. 2016 Feb 17;10:38. eCollection 2016.

Retinal Remodeling: Concerns, Emerging Remedies and Future Prospects.

Krishnamoorthy V, Cherukuri P, Poria D, Goel M, Dagar S, Dhingra NK.

Abstract: Deafferentation results not only in sensory loss, but also in a variety of alterations in the postsynaptic circuitry. These alterations may have detrimental impact on potential treatment strategies. Progressive loss of photoreceptors in retinal degenerative diseases, such as retinitis pigmentosa and age-related macular degeneration, leads to several changes in the remnant retinal circuitry. Müller glial cells undergo hypertrophy and form a glial seal. The second- and third-order retinal neurons undergo morphological, biochemical and physiological alterations. A result of these alterations is that retinal ganglion cells (RGCs), the output neurons of the retina, become hyperactive and exhibit spontaneous, oscillatory bursts of spikes. This aberrant electrical activity degrades the signal-to-noise ratio in RGC responses, and thus the quality of information they transmit to the brain. These changes in the remnant retina, collectively termed "retinal remodeling", pose challenges for genetic, cellular and bionic approaches to restore vision. It is therefore crucial to understand the nature of retinal remodeling, how it affects the ability of remnant retina to respond to novel therapeutic strategies, and how to ameliorate its effects. In this article, we discuss these topics, and suggest that the pathological state of the retinal output following photoreceptor loss is reversible, and therefore, amenable to restorative strategies.

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Free Radic Biol Med. 2016 Feb 23. [Epub ahead of print]

Malondialdehyde induces autophagy dysfunction and VEGF secretion in the retinal pigment epithelium in age-related macular degeneration.

Ye F, Kaneko H, Hayashi Y, Takayama K, Hwang SJ, Nishizawa Y, Kimoto R, Nagasaka Y, Tsunekawa T, Matsuura T, Yasukawa T, Kondo T, Terasaki H.

Abstract: Age-related macular degeneration (AMD) is a major cause of blindness in developed countries and is closely related to oxidative stress, which leads to lipid peroxidation. Malondialdehyde (MDA) is a major byproduct of polyunsaturated fatty acid (PUFA) peroxidation. Increased levels of MDA have been reported in eyes of AMD patients. However, little is known about the direct relationship between MDA and AMD. Here we show the biological importance of MDA in AMD pathogenesis. We first confirmed that MDA levels were significantly increased in eyes of AMD patients. In ARPE-19 cells, a human retinal pigment epithelial cell line, MDA treatment induced vascular endothelial growth factor (VEGF) expression alternation, cell junction disruption, and autophagy dysfunction that was also observed in eyes of AMD patients. The MDA-induced VEGF increase was inhibited by autophagy-lysosomal inhibitors. Intravitreal MDA injection in mice increased laser-induced choroidal neovascularization (laser-CNV) volumes. In a mouse model fed a high-linoleic acid diet for 3 months, we found a significant increase in MDA levels, autophagic activity, and laser-CNV volumes. Our study revealed an important role of MDA, which acts not only as a marker but also as a causative factor of AMD pathogenesis-related autophagy dysfunction. Furthermore, higher dietary intake of linoleic acid promoted CNV progression in mice with increased MDA levels.

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Ophthalmic Physiol Opt. 2016 Feb 29. [Epub ahead of print]

Preserved retinotopic brain connectivity in macular degeneration.

Haak KV, Morland AB, Rubin GS, Cornelissen FW.

PURPOSE: The eye disease macular degeneration (MD) is a leading cause of blindness worldwide. There is no cure for MD, but several promising treatments aimed at restoring vision at the level of the retina are currently under investigation. These treatments assume that the patient's brain can still process appropriately the retinal input once it is restored, but whether this assumption is correct has yet to be determined.

METHODS: We used functional magnetic resonance imaging (fMRI) and connective field modelling to determine whether the functional connectivity between the input-deprived portions of primary visual cortex (V1) and early extrastriate areas (V2/3) is still retinotopically organised. Specifically, in both patients with juvenile macular degeneration and age-matched controls with simulated retinal lesions, we assessed the extent to which the V1-referred connective fields of extrastriate voxels, as estimated on the basis of spontaneous fMRI signal fluctuations, adhered to retinotopic organisation.

RESULTS: We found that functional connectivity between the input-deprived portions of visual areas V1 and extrastriate cortex is still largely retinotopically organised in MD, although on average less so than in controls. Patients with stable fixation exhibited normal retinotopic connectivity, however, suggesting that for the patients with unstable fixation, eye-movements resulted in spurious, homogeneous signal modulations across the entire input-deprived cortex, which would have hampered our ability to assess their spatial structure of connectivity.

CONCLUSIONS: Despite the prolonged loss of visual input due to MD, the cortico-cortical connections of input-deprived visual cortex remain largely intact. This suggests that the restoration of sight in macular degeneration can rely on a largely unchanged retinotopic representation in early visual cortex following loss of central retinal function.

PMID: 26923706 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2016 Mar 1. [Epub ahead of print]

Increased choroidal mast cells and their degranulation in age-related macular degeneration.

Bhutto IA, McLeod DS, Jing T, Sunness JS, Seddon JM, Luty GA.

BACKGROUND/AIMS: Inflammation has been implicated in age-related macular degeneration (AMD). This study investigates the association of mast cells (MCs), a resident choroidal inflammatory cell, with pathological changes in AMD.

METHODS: Human donor eyes included aged controls (n=10), clinically diagnosed with early AMD (n=8), geographic atrophy (GA, n=4) and exudative AMD (n=11). The choroids were excised and incubated for alkaline phosphatase (APase; blood vessels) and non-specific esterase activities (MCs). Degranulated (DG) and non-degranulated MCs in four areas of posterior choroid (nasal, non-macular, paramacular and submacular) were counted in flat mounts (4-6 fields/area). Choroids were subsequently embedded in JB-4 and sectioned for histological analyses.

RESULTS: The number of MCs was significantly increased in all choroidal areas in early AMD ($p=0.0006$) and in paramacular area in exudative AMD (139.44 ± 55.3 cells/mm²; $p=0.0091$) and GA (199.08 ± 82.0 cells/mm²; $p=0.0019$) compared with the aged controls. DG MCs were also increased in paramacular ($p=0.001$) and submacular choroid ($p=0.02$) in all forms of AMD. Areas with the greatest numbers of DG MCs had loss of choriocapillaris (CC). Sections revealed that the MCs were widely distributed in Sattler's and Haller's layer in the choroidal stroma in aged controls, whereas MCs were frequently found in close proximity with CC in GA and exudative AMD and in choroidal neovascularisation (CNV).

CONCLUSION: Increased MC numbers and degranulation were observed in all AMD choroids. These results suggest that MC degranulation may contribute to the pathogenesis of AMD: death of CC and retinal pigment epithelial and CNV formation. The proteolytic enzymes released from MC granules may result in thinning of AMD choroid.

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Mol Med Rep. 2016 Feb 15. [Epub ahead of print]

TLR4 inhibitor attenuates amyloid- β -induced angiogenic and inflammatory factors in ARPE-19 cells: Implications for age-related macular degeneration.

Chen L, Bai Y, Zhao M, Jiang Y.

Abstract: Subretinally-deposited amyloid- β (A β) is an important factor in age-related macular degradation (AMD) often leading to irreversible blindness in the elderly population. The molecular mechanism underlying A β deposition during AMD remains unclear. The expression of inflammatory and angiogenic factors was examined by treatment of retinal pigment epithelial (RPE) cells with the oligomeric form of A β (OA β 1-42). Changes in the mRNA expression levels of various cytokines was detected by the QuantiGenePlex 6.0 Reagent system, and the protein expression level was determined by western blotting. Culture supernatants were detected using a multiplex cytokine assay and enzyme-linked immunosorbent assays. The in vitro tube formation was evaluated by a Matrigel assay. The present study highlights that OA β 1-42 activates the toll-like receptor 4 (TLR4), myeloid differentiation factor 88 and phosphorylation nuclear factor- κ B signaling pathway in RPE cells. Additionally, it increased the mRNA and protein expression of interleukin (IL)-6, IL-8, IL-33, vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF) and angiopoietin 2. Furthermore, the TLR4 inhibitor (COBRA) attenuated the expression of inflammatory and angiogenesis factors, particularly IL-6, IL-8, IL-33, bFGF and VEGF. When human umbilical vein endothelial cells (HUVECs) were co-cultured with the COBRA-treated RPE cell culture supernatant the length of the endothelial cell network (measured by calculating tip cell lengths of

endothelial cells) was impaired when compared with the HUVECs that were co-cultured with the cell supernatant exposed to OA β 1-42. These results suggest that the TLR4-associated pathway may be a potential target for the treatment of AMD.

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Epidemiology

Asia Pac J Ophthalmol (Phila). 2016 Mar 2. [Epub ahead of print]

The Global Issue of Vision Loss and What We Can Do About It José Rizal Medal 2015.

Taylor HR.

Abstract: The prevalence of blindness increases rapidly with increasing age. Globally, there are some 32 million people who are blind and 191 million with poor vision. The leading cause of blindness worldwide is cataract, whereas uncorrected refractive error causes most poor vision. The rates of blindness from diabetes and macular degeneration are rapidly increasing, and age-related macular degeneration is the leading cause of blindness in developed countries. Three quarters of this blindness can be prevented or treated, and although the absolute number of blind people increased slightly between 1990 and 2010, very importantly, the prevalence of blindness has been halved as eye care programs and particularly cataract services have developed. We know how to deliver better eye care, and it works! However, with only 205,000 ophthalmologists worldwide, there is much work to do. The International Council of Ophthalmology has a major focus on education and team building to improve the quality and availability of eye care around the world. Its programs include curricula for all levels, examinations, fellowships, teaching of teachers, continuing professional development, and of course, the World Ophthalmology Congresses. We must work together in partnership to eliminate avoidable blindness worldwide.

PMID: 26939111 [PubMed - as supplied by publisher]

JAMA. 2016 Mar 1;315(9):915-33.

Screening for Impaired Visual Acuity in Older Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force.

Chou R, Dana T, Bougatsos C, Grusing S, Blazina I.

IMPORTANCE: Impaired visual acuity is common among older adults and can adversely affect function and quality of life.

OBJECTIVE: To update a 2009 systematic review on screening for impaired visual acuity among older adults for the US Preventive Services Task Force (USPSTF).

DATA SOURCES: Ovid MEDLINE (2008 to January 2016), Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews.

STUDY SELECTION: Randomized clinical trials of screening; diagnostic accuracy studies of screening tests in primary care settings; and randomized clinical trials of treatment vs placebo or no treatment for uncorrected refractive errors, cataracts, and dry (atrophic) or wet (exudative) age-related macular degeneration (AMD). Studies of screening and diagnostic accuracy were limited to asymptomatic adults 65 years or older; studies of treatment included asymptomatic adults of any age.

DATA EXTRACTION AND SYNTHESIS: One investigator abstracted data, a second checked data for accuracy, and 2 investigators independently assessed study quality using predefined criteria. Random-effects meta-analysis was used to estimate the relative and absolute benefits of vascular endothelial growth factor inhibitors (anti-VEGF) for wet AMD.

MAIN OUTCOMES AND MEASURES: Visual acuity, vision-related function, functional capacity, harms, and diagnostic accuracy.

RESULTS: Three trials ($n = 4728$) from the 2009 USPSTF review found that screening for impaired visual acuity was not associated with improved visual or clinical outcomes. In 1 good-quality trial ($n = 3346$), universal screening identified 27% of persons with impaired visual acuity and correctable impairment vs 3.1% with targeted screening, but there was no difference in the likelihood of visual acuity worse than 20/60 after 3 to 5 years (37% vs 35%; relative risk [RR], 1.07; 95% CI, 0.84-1.36). The 2009 review found that effective treatments are available for uncorrected refractive errors and cataracts. Ten-year trial results of dry AMD found an antioxidant/zinc combination was associated with decreased risk of visual acuity loss (46% vs 54%; odds ratio, 0.71; 95% CI, 0.57-0.88). An updated meta-analysis found anti-VEGF for wet AMD was associated with greater likelihood of having vision 20/200 or better vs sham injection (4 trials; RR, 1.47; 95% CI, 1.30-1.66; I² = 42%; absolute risk difference, 24%; 95% CI, 12%-37% after 1 year). New evidence on the diagnostic accuracy of visual acuity screening tests was limited and consistent with previous findings that screening questions or a visual acuity test was associated with suboptimal accuracy.

CONCLUSIONS AND RELEVANCE: Screening can identify persons with impaired visual acuity, and effective treatments are available for common causes of impaired visual acuity, such as uncorrected refractive error, cataracts, and dry or wet AMD. However, direct evidence found no significant difference between vision screening in older adults in primary care settings vs no screening for improving visual acuity or other clinical outcomes.

Comment in

Visual Acuity Screening Among Asymptomatic Older Adults. [JAMA. 2016]

PMID: 26934261 [PubMed - in process]

Acta Ophthalmol. 2016 Mar 1. [Epub ahead of print]

Prevalence and associations of central serous chorioretinopathy in elderly Chinese. The Beijing Eye Study 2011.

Li Y, You QS, Wei WB, Xu J, Chen CX, Wang YX, Xu L, Jonas JB.

PURPOSE: To determine the prevalence and associations of central serous chorioretinopathy (CSC) in elderly Chinese.

METHODS: The population-based cross-sectional Beijing Eye Study 2011 included 3468 individuals (age: 64.6 ± 9.8 years; range: 50-93 years), who underwent enhanced depth imaging of spectral-domain optical coherence tomography (SD-OCT). CSC was defined as serous detachment of the retina in the macular region without signs of haemorrhages or signs of polypoidal choroidal vasculopathy, exudative age-related macular degeneration or other retinal vascular disorders, both on fundus photographs and on optical coherence tomography (OCT) images.

RESULTS: Central serous chorioretinopathy was diagnosed in 10 eyes (prevalence rate: $0.15 \pm 0.05\%$; 95% confidence interval (CI): 0.06%, 0.25%) of 10 subjects (prevalence rate: $0.31 \pm 0.10\%$; 95% CI: 0.12%, 0.50%). In five subjects, CSC was located foveally, and in five subjects, CSC was located extrafoveally. All subjects affected by foveal CSC were men, and three of the five individuals with extrafoveal CSC were men. In univariate analysis, subjects with CSC were significantly younger than the remaining study participants, and foveal CSC showed a significant ($p = 0.02$) predilection for men. After adjusting for age and gender, individuals with foveal CSC ($383 \pm 112 \mu\text{m}$ versus $270 \pm 47 \mu\text{m}$; $p = 0.02$) and the whole group of subjects with CSC had a significantly thicker subfoveal choroid. In a parallel manner, eyes contralateral to eyes with foveal CSC showed a significantly thicker subfoveal choroid than the age-adjusted control group ($413 \pm 74 \mu\text{m}$ versus $270 \pm 47 \mu\text{m}$; $p = 0.001$).

CONCLUSIONS: In Chinese aged 50+ years, the prevalence of CSC was 0.14% per subject. The choroid

in the CSC affected eyes and in the contralateral unaffected eyes was significantly thicker than in an age- and gender-adjusted control population-based group.

PMID: 26928876 [PubMed - as supplied by publisher]

JAMA. 2016 Mar 1;315(9):908-14.

Screening for Impaired Visual Acuity in Older Adults: US Preventive Services Task Force Recommendation Statement.

US Preventive Services Task Force (USPSTF), Siu AL, Bibbins-Domingo K, Grossman DC, et al

DESCRIPTION: Update of the US Preventive Services Task Force (USPSTF) recommendation on screening for impaired visual acuity in older adults.

METHODS: The USPSTF reviewed the evidence on screening for visual acuity impairment associated with uncorrected refractive error, cataracts, and age-related macular degeneration among adults 65 years or older in the primary care setting; the benefits and harms of screening; the accuracy of screening; and the benefits and harms of treatment of early vision impairment due to uncorrected refractive error, cataracts, and age-related macular degeneration.

POPULATION: This recommendation applies to asymptomatic adults 65 years or older who do not present to their primary care clinician with vision problems.

RECOMMENDATION: The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for impaired visual acuity in older adults. (I statement).

Comment in

Visual Acuity Screening Among Asymptomatic Older Adults. [JAMA. 2016]

PMID: 26934260 [PubMed - in process]

Genetics

Ophthalmic Genet. 2016 Mar 4:1-3. [Epub ahead of print]

Evaluation of CFH Y402H polymorphism and CFHR3/CFHR1 deletion in age-related macular degeneration patients from Brazil.

Saconi DP, Vasconcellos JP, Hirata FE, Medina FM, Rim PH, Melo MB.

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Diet, lifestyle and low vision

Nurs Older People. 2016 Jan;28(1):13.

Reducing depression and anxiety in visually impaired older people.

[No authors listed]

Abstract: Impaired vision, from conditions such as macular degeneration or glaucoma, is an important cause of age-related disability. Depression and anxiety are common in visually impaired adults and can lead to increased disability, decreased quality of life, decline in health status and even mortality.

PMID: 26938602 [PubMed - in process]

Int J Med Sci. 2016 Feb 3;13(2):139-46. eCollection 2016.

Melissa Officinalis L. Extracts Protect Human Retinal Pigment Epithelial Cells against Oxidative Stress-Induced Apoptosis.

Jeung IC, Jee D, Rho CR, Kang S.

BACKGROUND: We evaluated the protective effect of ALS-L1023, an extract of *Melissa officinalis* L. (Labiatae; lemon balm) against oxidative stress-induced apoptosis in human retinal pigment epithelial cells (ARPE-19 cells).

METHODS: ARPE-19 cells were incubated with ALS-L1023 for 24 h and then treated with hydrogen peroxide (H₂O₂). Oxidative stress-induced apoptosis and intracellular generation of reactive oxygen species (ROS) were assessed by flow cytometry. Caspase-3/7 activation and cleaved poly ADP-ribose polymerase (PARP) were measured to investigate the protective role of ALS-L1023 against apoptosis. The protective effect of ALS-L1023 against oxidative stress through activation of the phosphatidylinositol 3-kinase/protein kinase B (PI3K/Akt) was evaluated by Western blot analysis.

RESULTS: ALS-L1023 clearly reduced H₂O₂-induced cell apoptosis and intracellular production of ROS. H₂O₂-induced oxidative stress increased caspase-3/7 activity and apoptotic PARP cleavage, which were significantly inhibited by ALS-L1023. Activation of the PI3K/Akt pathway was associated with the protective effect of ALS-L1023 on ARPE-19 cells.

CONCLUSIONS: ALS-L1023 protected human RPE cells against oxidative damage. This suggests that ALS-L1023 has therapeutic potential for the prevention of dry age-related macular degeneration.

PMID: 26941573 [PubMed - in process]

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