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Drug treatment

Ophthalmic Surg Lasers Imaging Retina. 2016 Jun 1;47(6):544-554.

Retina Specialists Treating Diabetic Macular Edema Recommend Different Approaches for Patients Than They Would Choose for Themselves.

Miller CG, Budoff G, Jeng-Miller KW, Fine HF, Roth DB, Prenner JL.

BACKGROUND AND OBJECTIVE: Prior investigation shows retina specialists may select different treatment for age-related macular degeneration for themselves than for a hypothetical patient. The authors sought to investigate whether a similar bias exists for treatment decisions by retina specialists with regard to diabetic macular edema (DME).

PATIENTS AND METHODS: Two surveys asked retina specialists to select treatment for hypothetical patients with DME or for themselves. In Survey 2, a distinction was drawn between a visual acuity (VA) of 20/40 or better and 20/50 or worse.

RESULTS: In Survey 1, 54% to 61% of respondents selected bevacizumab (Avastin; Genentech, South San Francisco, CA) for patients and 36% to 40% selected the drug for themselves ($P < .0004$). It was found that 14% to 17% selected aflibercept (Eylea; Regeneron, Tarrytown, NY) for patients versus 31% to 38% who selected it for themselves ($P < .0001$). For a VA of 20/40 or better, 42% to 50% selected bevacizumab for their patients versus 32% to 39% ($P < .0005$) for themselves, and 20% to 23% selected aflibercept for patients versus 39% to 48% ($P < .0007$) for themselves. For a VA of 20/50 or worse, 24% to 28% chose bevacizumab for patients versus 17% to 20% for themselves (P value was not significant), and 59% to 66% selected aflibercept for their patients versus 66% to 78% for themselves ($P < .05$).

CONCLUSION: Physicians recommend different treatment for their patients than for themselves, though not for a VA of 20/50 or worse, where data support the use of aflibercept over bevacizumab.

PMID: 27327284 [PubMed - as supplied by publisher]

Ophthalmology. 2016 Jun 9. [Epub ahead of print]

Predictors of Outcome in Patients with Neovascular Age-Related Macular Degeneration Switched from Ranibizumab to 8-Weekly Aflibercept.

Chatziralli I, Nicholson L, Vrizidou E, Koutsouki C, Menon D, Sergentanis TN, Citu MC, Hamilton R, Patel PJ, Hykin P, Sivaprasad S.

PURPOSE: The purpose of this study was to evaluate the outcomes over 12 months in patients with neovascular age-related macular degeneration (nAMD) with insufficient response to ranibizumab who were switched directly to 8-weekly fixed dosing of aflibercept without a loading phase.

DESIGN: Retrospective interventional study.

PARTICIPANTS: Consecutive patients with nAMD who were switched from pro re nata (PRN) intravitreal ranibizumab to 8-weekly fixed aflibercept because of persistent disease activity from November 1, 2013, to September 30, 2014, were included.

METHODS: Demographic data, visual acuity (VA), and spectral-domain optical coherence tomography characteristics over time were evaluated to determine the prognostic indicators of final visual outcome at 12 months.

MAIN OUTCOME MEASURES: The VA, central subfield thickness (CST), presence of macular fluid at month 12 compared with baseline, and the definition of prognostic indicators of final visual outcome at month 12.

RESULTS: A total of 431 patients (447 eyes) were included in this study. There was no statistically significant difference in VA between baseline and month 12 ($P = 0.79$), whereas the CST significantly decreased at month 12 compared with baseline ($P < 0.001$). At the 12-month follow-up, 48.3% of eyes had no macular fluid compared with 8.5% at baseline. The mean number of injections at month 12 was 6.8 ± 1.75 . Poor prognostic indicators included increasing age, increasing CST, the presence of intraretinal fluid, pigment epithelial detachment, and subfoveal thickening.

CONCLUSIONS: Patients who have not yet "responded" to PRN ranibizumab seem to exhibit retinal dehydration after switching to aflibercept, whereas there was no demonstration of VA benefit. Baseline features at the point of switching can independently predict outcomes.

PMID: 27289179 [PubMed - as supplied by publisher]

Patient Prefer Adherence. 2016 May 26;10:949-55. eCollection 2016.

Treatment satisfaction of patients undergoing ranibizumab therapy for neovascular age-related macular degeneration in a real-life setting.

Gohil R, Crosby-Nwaobi R, Forbes A, Burton BJ, Hykin P, Sivaprasad S.

CONTEXT: Treatment satisfaction with a loading phase of monthly injections for 3 months followed by a pro-re-nata regimen of ranibizumab in neovascular age-related macular degeneration (nAMD) remains unclear.

AIMS: The aim was to evaluate the treatment satisfaction of persons with nAMD treated with ranibizumab in a real-life setting.

SETTINGS AND DESIGN: A cross-sectional study was conducted across three eye clinics within the National Health Service in the UK, where treatment is provided free at point of contact.

MATERIALS AND METHODS: A total of 250 patients were selected randomly for the study. Treatment satisfaction was assessed using the Macular Treatment Satisfaction Questionnaire. Data were collected on satisfaction of the service provided (Client Service Questionnaire-8) and the patients' demographic and quality of life and treatment history. Factors governing treatment questionnaire were determined.

RESULTS: The most important factors that determined the satisfaction were the service provided at the clinic (Client Service Questionnaire-8), health-related quality of life (EQ-5D-3L), and duration of AMD. Visual acuity changes were rated as less important than one would have expected.

CONCLUSION: The study result suggested that treatment satisfaction for nAMD was governed by the perception of being reviewed and injected regularly over a long period of time than the actual change in visual acuity from the treatment.

PMID: 27307715 [PubMed] PMCID: PMC4889099

Ophthalmic Surg Lasers Imaging Retina. 2016 Jun 1;47(6):536-543.

Comparison of Ranibizumab 0.5 mg Versus 1.0 mg for the Treatment of Patients With Clinically Significant Diabetic Macular Edema: A Randomized, Clinical Trial.

Ferrone PJ, Jonisch J.

BACKGROUND AND OBJECTIVE: To compare ranibizumab (Lucentis; Genentech, South San Francisco, CA) 0.5 mg and 1.0 mg for the treatment of clinically significant diabetic macular edema (CSDME).

PATIENTS AND METHODS: This was a 12-month, prospective, single-masked, randomized clinical trial. Patients with CSDME secondary to diabetic retinopathy were randomized to receive 0.5 mg or 1.0 mg of ranibizumab by intravitreal injection once monthly for 3 months and then once every other month as needed.

RESULTS: Patients received a mean of 6.5 injections in each group during the course of this 12-month study. The mean change in Early Treatment Diabetic Retinopathy Study visual acuity from baseline to month 12 was +3.8 letters in the ranibizumab 0.5-mg group (n = 23) and +7.9 letters in the 1.0-mg group (n = 23; P = .92 vs. 0.5 mg). Central foveal thickness (CFT) significantly decreased from baseline to month 12 in both dose groups.

CONCLUSION: Treatment of CSDME with ranibizumab resulted in a statistically significant improvement in visual acuity (ranibizumab 1.0 mg) and decrease in CFT and macular volume (ranibizumab 0.5 mg and 1.0 mg) from baseline to 12 months. [Ophthalmic Surg Lasers Imaging Retina. 2016;47:536-543.].

PMID: 27327283 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2016 May 26;10:969-77. eCollection 2016.

One-year outcome of intravitreal aflibercept injection for age-related macular degeneration resistant to ranibizumab: rapid morphologic recovery and subsequent visual improvement.

Hirakata T, Fujinami K, Watanabe K, Sasaki M, Noda T, Akiyama K.

OBJECTIVE: To describe the 1-year efficacy of aflibercept in Japanese patients with age-related macular degeneration (AMD) who were resistant to ranibizumab treatment.

DESIGN: Retrospective case series.

PARTICIPANTS: Fourteen consecutive eyes of 14 patients with AMD were enrolled who had no substantial response or developed resistance to intravitreal ranibizumab injections.

METHODS: All patients were subcategorized into one of two subtypes of AMD: seven patients with occult choroidal neovascularization (CNV) and seven with polypoidal choroidal vasculopathy (PCV). Serial intravitreal aflibercept (IVA) injections were administered. Comprehensive ophthalmic examinations, including optical coherence tomography, were conducted at baseline and at follow-up examinations at 1, 3, 6, and 12 months after the initial IVA injection. The best-corrected visual acuity converted to logarithm of the minimum angle of resolution (logMAR) and central macular thickness (CMT) at each follow-up visit were compared with the baseline values. The anatomic response was also assessed with absorption or reduction of fluid in the subretina or subretinal pigment epithelial space.

RESULTS: The logMAR best-corrected visual acuity improved significantly at 3, 6, and 12 months in the total cohort: at 3 and 6 months in patients with occult CNV and at 3 and 12 months in patients with PCV. The CMT decreased significantly at all follow-up visits in the total cohort as well as in both subtypes, except for the CMT at 6 months in PCV patients. The anatomic improvement was also demonstrated in all cases, and pigment epithelial detachments tended to be resolved more rapidly in patients with PCV than in patients with occult CNV.

CONCLUSION: Conversion to IVA was effective in patients with AMD resistant to ranibizumab, showing rapid morphologic improvement. The logMAR visual acuity was raised significantly within 12 months, and

the clinical course of visual acuity improvement may differ according to the AMD subtypes.

PMID: 27307700 [PubMed] PMCID: PMC4888727

Expert Opin Drug Deliv. 2016 Jun 13. [Epub ahead of print]

Extended duration strategies for the pharmacologic treatment of diabetic retinopathy: Current status and future prospects.

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

INTRODUCTION: Intraocular pharmacotherapy (vascular endothelial growth factor [VEGF] inhibitors and corticosteroids) has become first-line therapy for diabetic retinopathy (DR). A series of intraocular injections is usually required before disease modulation decreases the treatment burden in some patients, but others with chronic diabetic macular edema may require intensive longer-term therapy.

AREAS COVERED: Recent studies showing successful pharmacologic treatment of proliferative DR will probably lead to increased use of pharmacotherapy, thereby further emphasizing the need for longer duration drugs. Recently approved anti-VEGF drugs (aflibercept) and corticosteroids (dexamethasone and fluocinolone inserts) provide extended durations of action. Longer action anti-VEGF molecules, sustained release devices and pumps, and encapsulated cell technology, may further decrease treatment burden, though regulatory approval may not occur for at least 5 years. Oral medications (danazol and minocycline) and modified topical drugs (loteprednol) will require daily administration but may decrease the frequency of visits to physicians' offices. Intravitreally administered drugs that target different biochemical pathways are being developed as monotherapy and combination therapy, and their effects on durability remains to be seen.

EXPERT OPINION: The rich development pipeline promises to provide improved therapeutic options in addition to drugs and devices with longer duration of action.

PMID: 27293138 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2016 Jun 16.[Epub ahead of print]

Comparison of time to retreatment and visual function between ranibizumab and aflibercept in age-related macular degeneration.

Inoue M, Yamane S, Sato S, Sakamaki K, Arakawa A, Kadonosono K.

PURPOSE: To compare time to retreatment and visual function between patients with treatment-naïve neovascular age-related macular degeneration (AMD) treated with either intravitreal ranibizumab (IVR) or intravitreal aflibercept (IVA) in routine clinical practice.

DESIGN: Retrospective, interventional comparative case series.

PARTICIPANTS: A total of 200 eyes of 197 patients with neovascular AMD.

METHODS: A total of 99 patients in the IVR group and 101 patients in the IVA group who met the inclusion criteria with 12 months of follow up were included in the present study. All patients received three consecutive monthly injections of 0.5 mg/0.05 mL ranibizumab or 2.0 mg/0.05 mL aflibercept as loading doses. Retreatment was allowed if evidence of clinical deterioration or the presence of intraretinal edema or subretinal fluid on spectral-domain optical coherence tomography examination performed at the 1-month follow-up was noted. The time to retreatment after the third injection during the loading phase to the first recurrence during the maintenance phase was compared between treatments using the Kaplan-Meier analysis. Functional and anatomical outcomes were also compared between the IVR and IVA groups.

RESULTS: The median time to retreatment after the last induction dose was 5 months in both groups. The

proportion of IVR patients who required injection retreatment was not significantly higher than that of IVA patients (67.7% and 63.4%, respectively, at the 12-month follow up; log rank test, $P = .554$). In both groups, significant improvements in postoperative best-corrected visual acuity (BCVA) compared with preoperative visual acuity was observed over the 12-month follow-up period ($P < .05$ for both). Central foveal thickness (CFT) decreased from the baseline values in both groups during the follow-up period ($P < .001$ for both). Although there was a trend toward greater BCVA improvements in the IVA group, no significant differences in BCVA or CFT were observed between the treatment groups.

CONCLUSIONS: Both IVR and IVA were well tolerated and demonstrated efficacy in improving the visual acuity in treatment-naïve patients with AMD. Despite a trend toward greater BCVA improvements in the IVA group, a similar injection burden was observed following the loading phases of both ranibizumab and aflibercept.

PMID: 27320059 [PubMed - as supplied by publisher]

Clin Exp Optom. 2016 Jun 19. [Epub ahead of print]

On the relationship between visual acuity and central retinal (macular) thickness after interventions for macular oedema in diabetics: a review.

Bong A, Doughty MJ, Button NF, Mansfield DC.

PURPOSE: The aim was to compare efficacy of treatments for diabetic macular oedema (DMO) from changes in visual acuity (VA) and central macular thickness (CMT).

METHODS: Peer-reviewed articles from 2004 to 2014 reporting intravitreal injections of bevacizumab (IVB), ranibizumab (IVR) or triamcinolone acetonide (IVTA) or laser photocoagulation therapy (LPT) provided data on pre-treatment (baseline) and final outcome measures. Net changes and relative changes (percentage) were assessed by linear regression analyses.

RESULTS: From 88 data sets the overall net change of VA was -0.10 ± 0.12 logMAR (mean $\pm$ standard deviation), being -0.13 ± 0.11 logMAR for IVB, 0 ± 0.08 logMAR for IVR and -0.12 ± 0.08 logMAR for IVTA as compared to 0.01 ± 0.14 logMAR for LPT. For CMT, the overall net change was -103 ± 71 microns, being -108 ± 64 microns for IVB, -182 ± 73 microns for IVR, and -102 ± 57 microns for IVTA and was -49 ± 60 microns for LPT. Overall, modest correlations were found between the absolute central retinal (macular) thickness change and the VA change, and the relative changes in these measures ($p < 0.001$, $r = 0.522$ or 0.457). The predicted visual outcome from a 100 microns reduction in CMT was -0.083 logMAR units, an effect not substantially influenced by the CMT measurement method.

CONCLUSIONS: Pharmacological treatment of DMO can be expected to result in a predictable decrease in CMT with an accompanying increase in VA, with the overall outcome being better than laser treatment.

PMID: 27320640 [PubMed - as supplied by publisher]

J Fr Ophtalmol. 2016 Jun 15. [Epub ahead of print]

[French practice patterns in the management of diabetic macular edema]. [Article in French]

Qu-Knafo L, Fajnkuchen F, Sarda V, Nghiem-Buffet S, Chaine G, Giocanti-Auregan A.

PURPOSE: To assess French practice patterns in the treatment of diabetic macular edema (DME).

METHODS: A 31-item survey investigating practice patterns in the diagnosis and management of DME was e-mailed in March 2015 to retina specialist members of the French-speaking Retina Specialist Society. During this time frame, only ranibizumab was reimbursed for this indication. For each question concerning the choice of treatments, respondents were asked to assume that all treatments having market approval were also reimbursed. Answers were analyzed anonymously by Evalandgo software.

RESULTS: Ninety-five specialists answered the survey. Two thirds of them initiated an intravitreal treatment for DME for a loss of vision greater than 0.5 (Monoyer scale). The three determining factors for treatment choice were potential VA improvement, expected retinal anatomic improvement, and patient availability for monthly follow-up. For central DME in phakic or pseudophakic eyes, the first choice of intravitreal (IVT) treatment was ranibizumab, even assuming that all drugs approved by French authorities (HAS) were reimbursed by the health care system. Eighty-five percent of retinal specialists propose bilateral intravitreal injections the same day for the same patient.

CONCLUSION: Most of the specialists initiate DME treatment for a VA>0.5 in France. Eighty-five percent of them perform bilateral intravitreal injections on the same day in the case of bilateral DME.

PMID: 27318630 [PubMed - as supplied by publisher]

Expert Opin Drug Deliv. 2016 Jun 16. [Epub ahead of print]

Ultrasound-mediated ocular delivery of therapeutic agents: a review.

Lafond M, Aptel F, Mestas JL, Lafon C.

INTRODUCTION: Due to numerous anatomical and physiological barriers, ocular drug delivery remains a major limitation in the treatment of diseases such as glaucoma, macular degeneration or inflammatory diseases. To date, only invasive approaches provide clinically effective results. Ultrasound can be defined as the propagation of a high-frequency sound wave exposing the propagation media to mechanical and thermal effects. Ultrasound has been proposed as a non-invasive physical agent for increasing therapeutic agent delivery in various fields of medicine.

AREAS COVERED: An update on recent advances in transscleral and transcorneal ultrasound-mediated drug delivery is presented. Efficient drug delivery is achieved in vitro, ex vivo and in vivo for various types of materials. Numerous studies indicate that efficacy is related to cavitation. Although slight reversible effects can be observed on the corneal epithelium, efficient drug delivery can be performed without causing damage to the cornea.

EXPERT OPINION: Recent developments prove the potential of ultrasound-mediated ocular drug delivery. Cavitation appears to be a preponderant mechanism, opening a way to treatment monitoring by cavitation measurement. Even if no clinical studies have yet been performed, the promising results summarized here are promoting developments toward clinical applications, particularly in assessing the safety of the technique.

PMID: 27310925 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging Retina. 2016 Jun 1;47(6):593-595.

Macular Telangiectasia Type 1 Managed With Long-Term Aflibercept Therapy.

Kovach JL, Hess H, Rosenfeld PJ.

Abstract: A 60-year-old man diagnosed with macular telangiectasia type 1 (MacTel 1) was treated for 3 years with monthly aflibercept (Eylea; Regeneron, Tarrytown, NY) and serially imaged with spectral-domain optical coherence tomography. When administered monthly, aflibercept appeared to have a beneficial effect on macular edema secondary to MacTel 1. Visual acuity preservation despite minimal chronic macular edema could be attributed to the lack of significant photoreceptor disruption.

PMID: 27327292 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2016 Jun 8. [Epub ahead of print]

Response of Pigment Epithelial Detachment to Anti-Vascular Endothelial Growth Factor Treatment in Age-Related Macular Degeneration.

Hanumunthadu D, Ilginis T, Balaggan KS, Patel PJ; DOCS Study team.

PMID: 27289398 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Doc Ophthalmol. 2016 Jun 11. [Epub ahead of print]

Electrophysiological and clinical tests in dry age-related macular degeneration follow-up: differences between mfERG and OCT.

González-García E, Vilela C, Navea A, Arnal E, Muriach M, Romero FJ.

BACKGROUND: Age-related macular degeneration (AMD) is one of the major causes of progressive and debilitating visual impairment in developed countries and has become a growing health and social issue that needs to be addressed. Imaging techniques and functional tests are useful to assess the degree of macular dysfunction and AMD progression. However, given the slow progression of the disease, it is necessary to identify which techniques are more sensitive for the diagnosis and monitoring of patients with AMD.

PURPOSE: To study changes observed with both imaging techniques and electrophysiological tests in dry AMD-diagnosed patients during 2 years in order to identify the most sensitive technique.

METHODS: Fundus photography, OCT (macular thickness and number of drusen), Pattern VEP (P100 wave), Pattern ERG (P50 wave) and multifocal ERG (central rings) were carried out in 30 patients that were diagnosed with dry AMD in both eyes. The tests were repeated 1 and 2 years later.

RESULTS: No statistically significant changes were observed in visual acuity or in the severity of the disease throughout the study. OCT showed an increase in the number of drusen, as well as in macular thickness. As for the electrophysiological techniques, no significant changes were observed throughout the study in Pattern VEP or Pattern ERG. mfERG showed significant alterations. Statistical analysis showed that mfERG is more efficient in detecting changes throughout the experimental period.

CONCLUSIONS: OCT and mfERG are useful in the diagnosis and monitoring of dry AMD patients, whilst mfERG is the most sensitive technique to study the progression of this disease in short periods of time.

PMID: 27290699 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging Retina. 2016 Jun 1;47(6):523-527.

Quantitative Characteristics of Spectral-Domain Optical Coherence Tomography in Corresponding Areas of Increased Autofluorescence at the Margin of Geographic Atrophy in Patients With Age-Related Macular Degeneration.

Hariri AH, Nittala MG, Sadda SR.

BACKGROUND AND OBJECTIVE: To evaluate the spectral-domain optical coherence tomography (SD-OCT) characteristics of the junctional zone corresponding to areas of increased autofluorescence (IAF) at the margin of geographic atrophy (GA) in patients with age-related macular degeneration (AMD).

PATIENTS AND METHODS: SD-OCT and fundus autofluorescence (FAF) images from untreated eyes with GA available from archived studies at Doheny Image Reading Center were evaluated. Areas of definite

decreased autofluorescence (DDAF) corresponding to GA, and areas of IAF at the margins of the GA were manually segmented. Eyes with evidence of IAF were selected. Following manual registration of FAF and OCT data, areas of IAF and normal fluorescence were correlated with OCT features at these locations.

RESULTS: Thirty eyes were included. The mean retinal pigment epithelium (RPE) thickness in areas of IAF was $40.6 \mu\text{m} \pm 7.69 \mu\text{m}$, compared to $28.8 \mu\text{m} \pm 7.09 \mu\text{m}$ in normal adjacent areas ($P < .001$).

CONCLUSION: Regions of IAF at the junctional zone of GA lesions appear to correspond to thickening of the presumed RPE band on OCT. [Ophthalmic Surg Lasers Imaging Retina. 2016;47:523-527.].

PMID: 27327281 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2016 Jun 10. [Epub ahead of print]

Photoreceptor Damage and Reduction of Retinal Sensitivity Surrounding Geographic Atrophy in Age-related Macular Degeneration.

Takahashi A, Ooto S, Yamashiro K, Oishi A, Tamura H, Nakanishi H, Ueda-Arakawa N, Tsujikawa A, Yoshimura N.

PURPOSE: To quantify the area of photoreceptor damage surrounding geographic atrophy (GA) and evaluate the relationship between structural abnormalities and retinal function in eyes with GA.

DESIGN: Prospective cross-sectional study.

METHODS: Twenty-five eyes of 25 patients with GA associated with age-related macular degeneration underwent a full ophthalmologic examination, including spectral-domain optical coherence tomography (SD-OCT), fundus autofluorescence (FAF), and microperimetry. ImageJ software was used to quantify the disruption of the ellipsoid zone on SD-OCT images. Hypofluorescent areas of the FAF images indicated areas of RPE loss. Areas of interest graded by SD-OCT (photoreceptor damage) and FAF (RPE loss) were registered with microperimetry within a 6-mm circle centered on the fovea.

RESULTS: The mean area of photoreceptor damage was $7.69 \pm 5.36 \text{ mm}^2$, which was significantly greater than the mean area of RPE loss ($4.57 \pm 4.07 \text{ mm}^2$, $P < 0.001$). The average retinal sensitivity of the area with photoreceptor damage outside the area of RPE loss was lower than that of the area without photoreceptor damage ($6.57 \pm 4.13 \text{ dB}$ vs $11.27 \pm 3.78 \text{ dB}$, $P < 0.001$). The area of photoreceptor damage surrounding the area of RPE loss was larger in eyes with pseudodrusen, than in eyes without pseudodrusen (4.96 mm^2 vs 1.91 mm^2 , $P = 0.008$). The only significant predictor of decreased retinal sensitivity was the area of the photoreceptor damage ($P < 0.001$).

CONCLUSIONS: Widespread photoreceptor damage surrounding sites of RPE loss occurred in eyes with GA, and it correlated with visual function. Evaluation of photoreceptor damage surrounding sites of RPE loss using OCT is important in patients with GA associated with AMD.

PMID: 27296489 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging Retina. 2016 Jun 1;47(6):517-522.

Artifactual Flow Signals Within Drusen Detected by OCT Angiography.

Zheng F, Roisman L, Schaal KB, Miller AR, Robbins G, Gregori G, Rosenfeld PJ.

BACKGROUND AND OBJECTIVE: To demonstrate possible flow artifacts when imaging drusen with optical coherence tomography angiography (OCTA).

PATIENTS AND METHODS: Patients with drusen were enrolled in a prospective OCT study using the Zeiss AngioPlex OCTA instrument (Carl Zeiss Meditec, Dublin, CA). Two kinds of en face slabs were

created for visualizing both structure and flow. The first slab followed the contour of Bruch's membrane. The second slab had an inner boundary following the retinal pigment epithelium (RPE) contour and an outer boundary following the contour of Bruch's membrane. The structure and flow signals from within the drusen were compared.

RESULTS: Eleven eyes of nine patients with age-related macular degeneration and drusen were imaged. In all 11 eyes, an artifactual flow signal was seen on the first slab where it intersected the RPE. This flow signal was a projection artifact from the overlying retinal vessels. The second slab did not show evidence of flow within drusen.

CONCLUSION: OCTA decorrelation projection artifacts can be misinterpreted as apparent flow within drusen if the slab region includes hyperreflective boundary layers such as the RPE. [Ophthalmic Surg Lasers Imaging Retina. 2016;47:517-522.].

PMID: 27327280 [PubMed - as supplied by publisher]

Telemed J E Health. 2016 Jun 21. [Epub ahead of print]

Eye Disease in Patients with Diabetes Screened with Telemedicine.

Park DW, Mansberger SL.

BACKGROUND: Telemedicine with nonmydriatic cameras can detect not only diabetic retinopathy but also other eye disease.

OBJECTIVE: To determine the prevalence of eye diseases detected by telemedicine in a population with a high prevalence of minority and American Indian/Alaskan Native (AI/AN) ethnicities.

SUBJECTS AND METHODS: We recruited diabetic patients 18 years and older and used telemedicine with nonmydriatic cameras to detect eye disease. Two trained readers graded the images for diabetic retinopathy, age-related macular degeneration (ARMD), glaucomatous features, macular edema, and other eye disease using a standard protocol. We included both eyes for analysis and excluded images that were too poor to grade.

RESULTS: We included 820 eyes from 424 patients with 72.3% nonwhite ethnicity and 50.3% AI/AN heritage. While 283/424 (66.7%) patients had normal eye images, 120/424 (28.3%) had one disease identified; 15/424 (3.5%) had two diseases; and 6/424 (1.4%) had three diseases in one or both eyes. After diabetic retinopathy (104/424, 24.5%), the most common eye diseases were glaucomatous features (44/424, 10.4%) and dry ARMD (24/424, 5.7%). Seventeen percent (72/424, 17.0%) showed eye disease other than diabetic retinopathy.

CONCLUSIONS: Telemedicine with nonmydriatic cameras detected diabetic retinopathy, as well as other visually significant eye disease. This suggests that a diabetic retinopathy screening program needs to detect and report other eye disease, including glaucoma and macular disease.

PMID: 27328169 [PubMed - as supplied by publisher]

Telemed J E Health. 2016 Jun 16. [Epub ahead of print]

Retrospective Evaluation of a Teleretinal Screening Program in Detecting Multiple Nondiabetic Eye Diseases.

Maa AY, Patel S, Chasan JE, Delaune W, Lynch MG.

BACKGROUND: Diabetic teleretinal screening programs have been utilized successfully across the world to detect diabetic retinopathy (DR) and are well validated. Less information, however, exists on the ability of teleretinal imaging to detect nondiabetic ocular pathology.

INTRODUCTION: This study performed a retrospective evaluation to assess the ability of a community-based diabetic teleretinal screening program to detect common ocular disease other than DR.

MATERIALS AND METHODS: A retrospective chart review of 1,774 patients who underwent diabetic teleretinal screening was performed. Eye clinic notes from the Veterans Health Administration's electronic medical record, Computerized Patient Record System, were searched for each of the patients screened through teleretinal imaging. When a face-to-face examination note was present, the physical findings were compared to those obtained through teleretinal imaging. Sensitivity, specificity, and positive and negative predictive values were calculated for suspicious nerve, cataract, and age-related macular degeneration.

RESULTS: A total of 903 patients underwent a clinical examination. The positive predictive value was highest for cataract (100%), suspicious nerve (93%), and macular degeneration (90%). The negative predictive value and the percent agreement between teleretinal imaging and a clinical examination were over 90% for each disease category.

DISCUSSION: A teleretinal imaging protocol may be used to screen for other common ocular diseases.

CONCLUSION: It may be feasible to use diabetic teleretinal photographs to screen patients for other potential eye diseases. Additional elements of the eye workup may be added to enhance accuracy of disease detection. Further study is necessary to confirm this initial retrospective review.

PMID: 27310867 [PubMed - as supplied by publisher]

Ophthalmology. 2016 Jun 16. pii: S0161-6420(16)30323-2. [Epub ahead of print]

Clinical Characteristics and Risk Factors of Extensive Macular Atrophy with Pseudodrusen: The EMAP Case-Control National Clinical Trial.

Douillard A, Picot MC, Delcourt C, et al

PURPOSE: To assess the association of clinical and biological factors with extensive macular atrophy with pseudodrusen (EMAP) characterized by bilateral macular atrophy occurring in patients aged 50 to 60 years and a rapid progression to legal blindness within 5 to 10 years.

DESIGN: A national matched case-control study.

PARTICIPANTS: Participants were recruited in 10 French Departments of Ophthalmology and their associated clinical investigation centers. All 115 patients with EMAP had symptoms before the age of 55 years due to bilateral extensive macular atrophy with a larger vertical axis and diffuse pseudodrusen. Three controls without age-related macular degeneration (AMD) or retinal disease at fundus examination were matched for each patient with EMAP by gender, age, and geographic area (in total 415).

METHODS: Subjects and controls underwent an eye examination including color, red-free autofluorescent fundus photographs and spectral-domain optical coherence tomography with macular analysis. The interviews collected demographic, lifestyle, family and personal medical history, medications, and biological data. Associations of risk factors were estimated using conditional logistic regression.

MAIN OUTCOME MEASURES: Extensive macular atrophy with pseudodrusen status (cases vs. controls).

RESULTS: Extensive macular atrophy with pseudodrusen most frequently affected women (70 women, 45 men). After multivariate adjustment, family history of glaucoma or AMD was strongly associated with EMAP (odds ratio [OR], 2.3, $P = 0.008$ and OR, 1.5, $P = 0.01$, respectively). No association was found with cardiac diseases or their risk factors. Mild and moderate kidney disease and higher neutrophil rate were associated with a reduced risk of EMAP (OR, 0.58, $P = 0.04$; OR, 0.34, $P = 0.01$; and OR, 0.59, $P = 0.003$, respectively). On the contrary, eosinophilia (OR, 1.6; $P = 0.0002$), lymphocytosis (OR, 1.84; $P = 0.0002$), increased erythrocyte sedimentation rate (OR, 6.5; $P = 0.0005$), decreased CH50 ($P = 0.001$), and high plasma C3 level ($P = 0.023$) were significantly associated with a higher risk of EMAP.

CONCLUSIONS: This study documents an association between EMAP and family history of AMD and glaucoma, a clear female predominance, and a systemic inflammatory profile. The reduced CH50 and increased C3 plasma values could reflect a more severe complement pathway dysfunction than in AMD, leading to early pseudodrusen and rapid development of geographic atrophy. There is no association of EMAP with AMD cardiac diseases or cardiac risks, including cigarette smoking.

PMID: 27320518 [PubMed - as supplied by publisher]

Lasers Surg Med. 2016 Jun 20. [Epub ahead of print]

Investigations into localized re-treatment of the retina with a 3-nanosecond laser.

Chidlow G, Plunkett M, Casson RJ, Wood JP.

BACKGROUND AND OBJECTIVES: Subvisual retinal lasers necessarily cause clinically invisible lesions, hence, they could intentionally or inadvertently be targeted at precisely the same or an overlapping location during repeat laser treatment. Herein, we investigated the structural integrity and cellular responses of localized re-treatment using a nanosecond laser (2RT) currently in trials for early age-related macular degeneration.

MATERIALS AND METHODS: Rats were randomly assigned to one of five groups: sham, subvisual 2RT, subvisual 2RT re-treatment, visual effect 2RT, visual effect 2RT re-treatment. Re-treatment groups were lasered on days 0 and 21; single laser groups were only lasered on day 21. All rats were euthanized at day 28 and eyes were then dissected and processed for immunohistochemistry. For re-treatment, the laser was targeted at precisely the same locations on both delivery occasions. Analytical endpoints included monitoring of retinal vascular integrity overlying lesions, investigation into any potential choroidal neovascularization, assessment of the RPE, quantification of collateral injury to photoreceptors or other neuronal classes, and delineation of glial reactivity.

RESULTS: Repeat laser administration to rats caused ostensibly identical retinal-RPE-choroid responses to those obtained in age-matched rats that received only a single application. Specifically, 7 days after treatment, RPE cells were re-populating lesion sites. No obvious consistent differences were evident between the single and repeat laser groups. Moreover, repeat laser caused no (measurable) additive injury to photoreceptors or other retinal neuronal classes from single laser treatment. In re-lasered animals, there was no increase in microglial activity overlying and adjacent to lesion sites relative to single lasered rats. Finally, there was no evidence of choroidal neovascularization after repeat laser treatment.

CONCLUSIONS: The overall results provide a measure of confidence that re-treatment of patients with 2RT should not provide any additional risk of developing visual scotomas, choroidal neovascularizations, or inflammatory events. Indeed, the collated results indicate that the metabolic and structural disruption to the RPE-retina caused by short pulse duration laser treatment is resolved within a short time frame such that re-treatment elicits a phenotype indistinguishable from single treatment. *Lasers Surg. Med.* © 2016 Wiley Periodicals, Inc.

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Can J Ophthalmol. 2016 Jun;51(3):233.

Peripapillary RNFL thickness in nonexudative versus chronically treated exudative age-related macular degeneration.

Kucukevcilioglu M, Aykas S, Hakan Durukan A.

PMID: 27316277 [PubMed - in process]

Pathogenesis

Invest Ophthalmol Vis Sci. 2016 Jun 1;57(7):3257-67.

Acute Stress Responses Are Early Molecular Events of Retinal Degeneration in Abca4^{-/-}Rdh8^{-/-} Mice After Light Exposure.

Parmar T, Parmar VM, Arai E, Sahu B, Perusek L, Maeda A.

PURPOSE: Mice lacking ATP-binding cassette transporter 4 (ABCA4) and retinol dehydrogenase 8 (RDH8) mimic features of human Stargardt disease and age-related macular degeneration. RNA-sequencing of whole eyes was done to study early gene expression changes in Abca4^{-/-}Rdh8^{-/-} mice.

METHODS: Abca4^{-/-}Rdh8^{-/-} mice at 4 weeks of age were exposed to intense light. Total RNA was extracted from whole eyes and used to generate RNA libraries that were paired-end sequenced on the Illumina HiSeq 2500 device. Differentially expressed genes were annotated using Gene set enrichment analysis (GSEA). Selected genes in enriched pathways exhibiting differential expression were validated using quantitative qRT-PCR and ELISA.

RESULTS: Transcriptome analysis of the whole eye identified 200 genes that were differentially expressed 24 hours after light exposure compared to no light in Abca4^{-/-}Rdh8^{-/-} mice. Expression of several visual cycle and photoreceptor genes were decreased, indicative of photoreceptor/RPE cell death. Gene categories of early stress response genes, inflammatory cytokines, immune factors, and JAK STAT components were upregulated. Lipocalin 2 (Lcn2) was the most upregulated early stress response gene identified. Protein LCN2 was produced by RPE cells and the neural retina after intense light exposure as well as in cultured RPE cells from mice and humans incubated with lipopolysaccharide or photoreceptor outer segments.

CONCLUSIONS: Identification of important mediators involved in the crosstalk between the acute stress response and immune activation in RPE cells and the neural retina, such as LCN2, provide novel molecular targets for reducing cellular stress during retinal degeneration.

PMID: 27315541 [PubMed - in process]

Int J Mol Sci. 2016 Jun 14;17(6).

All-Trans Retinoic Acid Modulates DNA Damage Response and the Expression of the VEGF-A and MKI67 Genes in ARPE-19 Cells Subjected to Oxidative Stress.

Tokarz P, Piastowska-Ciesielska AW, Kaarniranta K, Blasiak J.

Abstract: Age-related macular degeneration (AMD) is characterized by the progressive degradation of photoreceptors and retinal pigment epithelium (RPE) cells. ARPE-19 is an RPE cell line established as an in vitro model for the study of AMD pathogenesis. Oxidative stress is an AMD pathogenesis factor that induces DNA damage. Thus, the oxidative stress-mediated DNA damage response (DDR) of ARPE-19 cells can be important in AMD pathogenesis. The metabolism of retinoids-which regulates cell proliferation, differentiation, and the visual cycle in the retina-was reported to be disturbed in AMD patients. In the present work, we studied the effect of all-trans retinoic acid (ATRA, a retinoid) on DDR in ARPE-19 cells subjected to oxidative stress. We observed that ATRA increased the level of reactive oxygen species (ROS), alkali-labile sites in DNA, DNA single-strand breaks, and cell death evoked by oxidative stress. ATRA did not modulate DNA repair or the distribution of cells in cell cycle in the response of ARPE-19 cells to oxidative stress. ATRA induced autophagy in the absence of oxidative stress, but had no effect on this process in the stress. ATRA induced over-expression of proliferation marker MKI67 and neovascularization marker VEGF-A. In conclusion, ATRA increased oxidative stress in ARPE-19 cells, resulting in more lesions to their DNA and cell death. Moreover, ATRA can modulate some properties of these cells, including neovascularization, which is associated with the exudative form of AMD. Therefore, ATRA can be important in the prevention, diagnosis, and therapy of AMD.

PMID: 27314326 [PubMed - in process]

J Drug Deliv. 2016;2016:7913616. Epub 2016 May 26.

Investigation of Diffusion Characteristics through Microfluidic Channels for Passive Drug Delivery Applications.

Goudie MJ, Ghuman AP, Collins SB, Pidaparti RM, Handa H.

Abstract: Microfluidics has many drug delivery applications due to the ability to easily create complex device designs with feature sizes reaching down to the 10s of microns. In this work, three different microchannel designs for an implantable device are investigated for treatment of ocular diseases such as glaucoma, age-related macular degeneration (AMD), and diabetic retinopathy. Devices were fabricated using polydimethylsiloxane (PDMS) and soft lithography techniques, where surface chemistry of the channels was altered using 2-[methoxy(polyethyleneoxy)propyl]trimethoxysilane (PEG-silane). An estimated delivery rate for a number of common drugs was approximated for each device through the ratio of the diffusion coefficients for the dye and the respective drug. The delivery rate of the model drugs was maintained at a physiological condition and the effects of channel design and surface chemistry on the delivery rate of the model drugs were recorded over a two-week period. Results showed that the surface chemistry of the device had no significant effect on the delivery rate of the model drugs. All designs were successful in delivering a constant daily dose for each model drug.

PMID: 27313895 [PubMed] PMCID: PMC4899604

J Cell Mol Med. 2016 Jun 16. [Epub ahead of print]

Methylglyoxal induces cell death through endoplasmic reticulum stress-associated ROS production and mitochondrial dysfunction.

Chan CM, Huang DY, Huang YP, Hsu SH, Kang LY, Shen CM, Lin WW.

Abstract: Diabetic retinopathy (DR) and age-related macular degeneration (AMD) are two important leading causes of acquired blindness in developed countries. As accumulation of advanced glycation end products (AGEs) in retinal pigment epithelial (RPE) cells plays an important role in both DR and AMD, and the methylglyoxal (MGO) within the AGEs exerts irreversible effects on protein structure and function, it is crucial to understand the underlying mechanism of MGO-induced RPE cell death. Using ARPE-19 as the cell model, this study revealed that MGO induces RPE cell death through a caspase-independent manner, which relying on reactive oxygen species (ROS) formation, mitochondrial membrane potential (MMP) loss, intracellular calcium elevation and endoplasmic reticulum (ER) stress response. Suppression of ROS generation can reverse the MGO-induced ROS production, MMP loss, intracellular calcium increase and cell death. Moreover, store-operated calcium channel inhibitors MRS1845 and YM-58483, but not the inositol 1,4,5-trisphosphate (IP3) receptor inhibitor xestospongin C, can block MGO-induced ROS production, MMP loss and sustained intracellular calcium increase in ARPE-19 cells. Lastly, inhibition of ER stress by salubrinal and 4-PBA can reduce the MGO-induced intracellular events and cell death. Therefore, our data indicate that MGO can decrease RPE cell viability, resulting from the ER stress-dependent intracellular ROS production, MMP loss and increased intracellular calcium increase. As MGO is one of the components of drusen in AMD and is the AGEs adduct in DR, this study could provide a valuable insight into the molecular pathogenesis and therapeutic intervention of AMD and DR.

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Invest Ophthalmol Vis Sci. 2016 Jun 1;57(7):3138-44.

Blockage of PI3K/mTOR Pathways Inhibits Laser-Induced Choroidal Neovascularization and Improves Outcomes Relative to VEGF-A Suppression Alone.

Ma J, Sun Y, López FJ, Adamson P, Kurali E, Lashkari K.

PURPOSE: Choroidal neovascularization (CNV) is a major cause of visual loss with age-related macular degeneration (AMD). We evaluated whether blockade of phosphatidyl-inositol-3-kinase (PI3K) and the mammalian target of rapamycin (mTOR), by impairing VEGF-A and other growth factor receptors like platelet-derived growth factor (PDGF), would reduce laser-induced CNV in mice.

METHODS: Choroidal neovascularization lesions were induced in C57BL/6 mice. Two groups of mice received oral GSK2126458 (3 mg/kg) or vehicle for 14 days following laser, whereas three groups were treated with GSK2126458 (6 µg/eye), aflibercept (2 µL/eye), or vehicle intravitreally on days 0 and 7 after laser. Vascular leakage was measured by fluorescein angiography (FA) on day 14. Choroidal neovascularization membranes were evaluated on choroidal flat mounts following FITC-dextran perfusion, as well as ED1 and isolectin B4 (IB4) immunohistochemistry.

RESULTS: Oral and intravitreal (IVT) GSK2126458 reduced leakage and area of CNV lesions. Greater probability of leaking lesions (~60%; $P < 0.05$) was observed in both vehicle groups. Fluorescein isothiocyanate-dextran-labeled total CNV burden area (total lesion area/eye) was reduced ~67% ($P < 0.05$) and 35% ($P = 0.0528$) after oral and IVT GSK2126458 administration. GSK2126458 treatment reduced lesion size by ~80% ($P < 0.05$) and 50% ($P < 0.05$) for oral and IVT control groups. Aflibercept did not alter lesion size (~27% reduction).

CONCLUSIONS: Phosphatidyl-inositol-3-kinase/mTOR is involved in laser-induced CNV angiogenic processes. GSK2126458 effectively reduces CNV size and leakage. Choroidal neovascularization size following IVT GSK2126458 was smaller than after oral administration. Therefore, inhibition of PI3K/mTOR pathways may be more effective due to blockade of action of multiple growth factors.

PMID: 27304845 [PubMed - in process]

Am J Pathol. 2016 Jun 11. [Epub ahead of print]

The Complement Regulatory Protein CD46 Deficient Mouse Spontaneously Develops Dry-Type Age-Related Macular Degeneration-Like Phenotype.

Lyzogubov VV, Bora PS, Wu X, Horn LE, de Roque R, Rudolf XV, Atkinson JP, Bora NS.

Abstract: In the mouse, membrane cofactor protein (CD46), a key regulator of the alternative pathway of the complement system, is only expressed in the eye and on the inner acrosomal membrane of spermatozoa. We noted that although Cd46^{-/-} mice have normal systemic alternative pathway activating ability, lack of CD46 leads to dysregulated complement activation in the eye, as evidenced by increased deposition of C5b-9 in the retinal pigment epithelium (RPE) and choroid. A knockout of CD46 induced the following cardinal features of human dry age-related macular degeneration (AMD) in 12-month-old male and female mice: accumulation of autofluorescent material in and hypertrophy of the RPE, dense deposits in and thickening of Bruch's membrane, loss of photoreceptors, cells in subretinal space, and a reduction of choroidal vessels. Collectively, our results demonstrate spontaneous age-related degenerative changes in the retina, RPE, and choroid of Cd46^{-/-} mice that are consistent with human dry AMD. These findings provide the exciting possibility of using Cd46^{-/-} mice as a convenient and reliable animal model for dry AMD. Having such a relatively straight-forward model for dry AMD should provide valuable insights into pathogenesis and a test model system for novel drug targets. More important, tissue-specific expression of CD46 gives the Cd46^{-/-} mouse model of dry AMD a unique advantage over other mouse models using knockout strains.

PMID: 27295359 [PubMed - as supplied by publisher]

Biomed Res Int. 2016;2016:2954721. Epub 2016 May 18.

Retinal Macrogial Responses in Health and Disease.

de Hoz R, Rojas B, Ramírez AI, Salazar JJ, Gallego BI, Triviño A, Ramírez JM.

Abstract: Due to their permanent and close proximity to neurons, glial cells perform essential tasks for the normal physiology of the retina. Astrocytes and Müller cells (retinal macroglia) provide physical support to neurons and supplement them with several metabolites and growth factors. Macroglia are involved in maintaining the homeostasis of extracellular ions and neurotransmitters, are essential for information processing in neural circuits, participate in retinal glucose metabolism and in removing metabolic waste products, regulate local blood flow, induce the blood-retinal barrier (BRB), play fundamental roles in local immune response, and protect neurons from oxidative damage. In response to polyetiological insults, glia cells react with a process called reactive gliosis, seeking to maintain retinal homeostasis. When malfunctioning, macroglial cells can become primary pathogenic elements. A reactive gliosis has been described in different retinal pathologies, including age-related macular degeneration (AMD), diabetes, glaucoma, retinal detachment, or retinitis pigmentosa. A better understanding of the dual, neuroprotective, or cytotoxic effect of macroglial involvement in retinal pathologies would help in treating the physiopathology of these diseases. The extensive participation of the macroglia in retinal diseases points to these cells as innovative targets for new drug therapies.

PMID: 27294114 [PubMed - in process] PMCID: PMC4887628

PLoS One. 2016 Jun 16;11(6):e0157748. eCollection 2016.

Retinal Inhibition of CCR3 Induces Retinal Cell Death in a Murine Model of Choroidal Neovascularization.

Wang H, Han X, Gambhir D, Becker S, Kunz E, Liu AJ, Hartnett ME.

Abstract: Inhibition of chemokine C-C motif receptor 3 (CCR3) signaling has been considered as treatment for neovascular age-related macular degeneration (AMD). However, CCR3 is expressed in neural retina from aged human donor eyes. Therefore, broad CCR3 inhibition may be harmful to the retina. We assessed the effects of CCR3 inhibition on retina and choroidal endothelial cells (CECs) that develop into choroidal neovascularization (CNV). In adult murine eyes, CCR3 colocalized with glutamine-synthetase labeled Müller cells. In a murine laser-induced CNV model, CCR3 immunolocalized not only to lectin-stained cells in CNV lesions but also to the retina. Compared to non-lasered controls, CCR3 mRNA was significantly increased in laser-treated retina. An intravitreal injection of a CCR3 inhibitor (CCR3i) significantly reduced CNV compared to DMSO or PBS controls. Both CCR3i and a neutralizing antibody to CCR3 increased TUNEL+ retinal cells overlying CNV, compared to controls. There was no difference in cleaved caspase-3 in laser-induced CNV lesions or in overlying retina between CCR3i- or control-treated eyes. Following CCR3i, apoptotic inducible factor (AIF) was significantly increased and anti-apoptotic factor BCL2 decreased in the retina; there were no differences in retinal vascular endothelial growth factor (VEGF). In cultured human Müller cells exposed to eotaxin (CCL11) and VEGF, CCR3i significantly increased TUNEL+ cells and AIF but decreased BCL2 and brain derived neurotrophic factor, without affecting caspase-3 activity or VEGF. CCR3i significantly decreased AIF in RPE/choroids and immunostaining of phosphorylated VEGF receptor 2 (p-VEGFR2) in CNV with a trend toward reduced VEGF. In cultured CECs treated with CCL11 and/or VEGF, CCR3i decreased p-VEGFR2 and increased BCL2 without increasing TUNEL+ cells and AIF. These findings suggest that inhibition of retinal CCR3 causes retinal cell death and that targeted inhibition of CCR3 in CECs may be a safer if CCR3 inhibition is considered as a therapy for neovascular AMD.

PMID: 27309355 [PubMed - in process]

PLoS One. 2016 Jun 16;11(6):e0157590. eCollection 2016.

Propofol Decreases Endoplasmic Reticulum Stress-Mediated Apoptosis in Retinal Pigment Epithelial Cells.

Zhou X, Wei Y, Qiu S, Xu Y, Zhang T, Zhang S.

Abstract: Age-related macular degeneration (AMD) is the major cause of loss of sight globally. There is currently no effective treatment available. Retinal pigment epithelial (RPE) cells are an important part of the outer blood-retina barrier and their death is a determinant of AMD. Propofol, a common clinically used intravenous anesthetic agent, has been shown to act as an efficacious neuroprotective agent with antioxidative and anti-inflammatory properties in vivo and in vitro. However, little is known about its effects on RPE cells. The purpose of our research was to investigate whether propofol could protect RPE cells from apoptosis through endoplasmic reticulum (ER) stress-dependent pathways. To this end, prior to stimulation with thapsigargin (TG), ARPE-19 cells were pretreated with varying concentrations of propofol. A protective effect of propofol in TG-treated ARPE-9 was apparent, TUNEL and flow cytometric assays showed decreased apoptosis. We further demonstrated that propofol pretreatment attenuated or inhibited the effects caused by TG, such as upregulation of Bax, BiP, C/EBP homologous protein (CHOP), active caspase 12, and cleaved caspase 3, and downregulation of Bcl2. It also decreased the TG-induced levels of ER stress-related molecules such as p-PERK, p-eIF2 α , and ATF4. Furthermore, it downregulated the expression of nuclear factor κ B (NF- κ B). This study elucidated novel propofol-induced cellular mechanisms for antiapoptotic activities in RPE cells undergoing ER stress and demonstrated the potential value of using propofol in the treatment of AMD.

PMID: 27311010 [PubMed - in process]

Genetics

Acta Ophthalmol. 2016 Jun 18. [Epub ahead of print]

Evaluation of CC-cytokine ligand 2 and complementary factor H Y402H polymorphisms and their interactional association with age-related macular degeneration.

Bonyadi M, Foruzandeh Z, Mohammadian T, Fotouhi N, Soheilian M, Jabbarpoor Bonyadi MH, Javadzadeh A, Moein H, Yaseri M.

PURPOSE: To evaluate the association of CC-cytokine ligand 2 CCL2-2518 (rs1024611) single nucleotide polymorphism, complement factor H (CFH Y402H) and their possible interaction in developing advanced age-related macular degeneration (AMD).

METHODS: In this case-control study, DNA samples from 266 patients with advanced AMD and 229 healthy controls were genotyped for CCL2 polymorphism and also 254 patients and 164 healthy controls were genotyped for CFH polymorphism. The possible associations of these polymorphisms with susceptibility to AMD independently and in different joint combinations were evaluated.

RESULTS: The genotype frequency for CFH was found to be significantly different between AMD and normal controls (31.5% versus 20.7%, OR = 3.56, $p < 0.001$ for CC and 52.4% versus 41.5%, OR = 2.96, $p < 0.001$ for CT genotype). However, no significant association between CCL2 polymorphism and AMD was observed in this cohort (OR = 1.15 and OR = 0.8, $p = 0.172$). Interestingly, studying the joint effects of two genotypes (TT genotype of CFH Y402H and AG genotype of CCL2-2518) showed more significant protective effect against AMD ($p = 0.0001$), while the risk effect of CC and CT genotypes of CFH was only visible in the presence of AA genotype of CCL2-2518 ($p = 0.044$ and $p = 0.05$).

CONCLUSION: Complement factor H Y402H polymorphism is strongly associated with advanced type AMD. Although this study revealed no association of CCL2-2518 with AMD, the risk effect of CFH genotypes was only visible in the presence of AA genotype of CCL2-2518. AG genotype of CCL2-2518 in combination with TT genotype of CFH Y402H showed significant protective effect against AMD.

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Diet, lifestyle & low vision

Clin Exp Optom. 2016 Jun 19. [Epub ahead of print]

An update on the characteristics of patients attending the Kooyong Low Vision Clinic.

Chong MF, Jackson AJ, Wolffsohn JS, Bentley SA.

BACKGROUND: Since 1972, the Australian College of Optometry has worked in partnership with Vision Australia to provide multidisciplinary low-vision care at the Kooyong Low Vision Clinic. In 1999, Wolffsohn and Cochrane reported on the demographic characteristics of patients attending Kooyong. Sixteen years on, the aim of this study is to review the demographics of the Kooyong patient cohort and prescribing patterns.

METHODS: Records of all new patients (n = 155) attending the Kooyong Low Vision Clinic for optometry services between April and September 2012 were retrospectively reviewed.

RESULTS: Median age was 84.3 years (range 7.7 to 98.1 years) with 59 per cent female. The majority of patients presented with late-onset degenerative pathology, 49 per cent with a primary diagnosis of age-related macular degeneration. Many (47.1 per cent) lived with their families. Mean distance visual acuity was 0.57 ± 0.47 logMAR or approximately 6/24. The median spectacle-corrected near visual acuity was N8 (range N3 to worse than N80). Fifty patients (32.3 per cent) were prescribed new spectacles, 51 (32.9 per cent) low vision aids and five (8.3 per cent) were prescribed electronic magnification devices. Almost two-thirds (63.9 per cent) were referred for occupational therapy management and 12.3 per cent for orientation and mobility services.

CONCLUSIONS: The profile of patients presenting for low-vision services at Kooyong is broadly similar to that identified in 1999. Outcomes appear to be similar, aside from an expected increase in electronic devices and technological solutions; however, the nature of services is changing, as treatments for ocular diseases advance and assistive technology develops and becomes more accessible. Alongside the aging population and age-related ocular disease being the predominant cause of low vision in Australia, the health-funding landscape is becoming more restrictive. The challenge for the future will be to provide timely, high-quality care in an economically efficient model.

PMID: 27320822 [PubMed - as supplied by publisher]

Nurs Older People. 2004 Dec 1;16(9):42.

Charles Bonnet syndrome - elderly people and visual hallucinations.

Sander R.

Abstract: Older people who report visual hallucinations are usually considered to be suffering from delusion or dementia. However, Charles Bonnet syndrome is characterised by hallucinations in people with failing eyesight and it is not necessarily associated with cognitive impairment. The syndrome is most commonly seen in older people. This is probably because they are most likely to have visual impairment from conditions such as macular degeneration, glaucoma and cataract. Hallucinations can be vivid and can last for minutes or hours.

PMID: 27319930 [PubMed]

Ophthalmologe. 2016 Jun 16. [Epub ahead of print]

[Internet search for counseling offers for older adults suffering from visual impairment]. [Article in German]

Himmelsbach I, Lipinski J, Putzke M.

BACKGROUND: Visual impairment is a relevant problem of aging. In many cases promising therapeutic options exist but patients are often left with visual deficits, which require a high degree of individualized counseling. This article analyzed which counseling offers can be found by patients and relatives using simple and routine searching via the internet.

METHOD: Analyses were performed using colloquial search terms in the search engine Google in order to find counseling options for elderly people with visual impairments available via the internet.

RESULTS: With this strategy 189 offers for counseling were found, which showed very heterogeneous regional differences in distribution. The counseling options found in the internet commonly address topics such as therapeutic interventions or topics on visual aids corresponding to the professions offering rehabilitation most present in the internet, such as ophthalmologists and opticians. Regarding contents addressing psychosocial and help in daily tasks, self-help and support groups offer the most differentiated and broadest spectrum. Support offers for daily living tasks and psychosocial counseling from social providers were more difficult to find with these search terms despite a high presence in the internet.

DISCUSSION: There are a large number of providers of counseling and consulting for older persons with visual impairment. In order to be found more easily by patients and to be recommended more often by ophthalmologists and general practitioners, the presence of providers in the internet must be improved, especially providers of daily living and psychosocial support offers.

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Carotenemia and Age-Related Macular Degeneration: Seeing Is Believing.

Heymann WR.

PMID: 27319957 [PubMed - in process]

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