Macular Disease Foundation AUSTRALIA
Our focus is your vision

MD Research News

Issue 253

Monday 19 October, 2015

This free weekly bulletin lists the latest published research articles on macular degeneration (MD) and some other macular diseases as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases.

If you have not already subscribed, please email Rob Cummins at **research@mdfoundation.com.au** with 'Subscribe to MD Research News' in the subject line, and your name and address in the body of the email.

You may unsubscribe at any time by an email to the above address with your 'unsubscribe' request.

Drug treatment

Ophthalmic Surg Lasers Imaging Retina. 2015 Oct 1;46(9):950-4.

Short-Term Outcomes of Aflibercept Therapy for Diabetic Macular Edema in Patients With Incomplete Response to Ranibizumab and/or Bevacizumab.

Wood EH, Karth PA, Moshfeghi DM, Leng T.

BACKGROUND AND OBJECTIVE: Aflibercept is a vascular endothelial growth factor (VEGF) inhibitor recently approved by the U.S. Food and Drug Administration for the treatment of diabetic macular edema (DME). Currently, the effect of switching to aflibercept from other anti-VEGF agents for DME is unknown.

PATIENTS AND METHODS: In this prospective, interventional case series, DME patients with persistent retinal fluid despite regular (every 4 to 6 weeks) intravitreal injection (IVI) with ranibizumab 0.3 mg, and/or bevacizumab 1.25 mg were switched to IVI aflibercept 2 mg. Collected data included visual acuity, central subfield foveal thickness (CSFT), and the area of thickest edema on registered spectral-domain optical coherence tomography (SD-OCT).

RESULTS: At 1 month after the first aflibercept IVI, 79% (11 of 14 eyes) showed anatomic improvement with a 23% decrease in average CSFT from 421 μm to 325 μm ($P < .0132$).

CONCLUSION: A majority of patients with DME with persistent fluid on SD-OCT despite regular ranibizumab 0.3 mg and/or bevacizumab 1.25 mg IVIs showed a positive anatomic response to IVI aflibercept 2 mg.

PMID: 26469235 [PubMed - in process]

Can J Ophthalmol. 2015 Oct;50(5):373-7. Epub 2015 Aug 12.

Aflibercept for pigment epithelial detachment for previously treated neovascular age-related macular degeneration.

Major JC Jr, Wykoff CC, Croft DE, Wang R, Mariani AF, Lehmann AE, Brown DM.

OBJECTIVE: Assess the efficacy of intravitreal aflibercept on pigment epithelial detachments (PED) associated with previously treated patients with neovascular age-related macular degeneration (AMD).

DESIGN: Retrospective study.

PARTICIPANTS: Sixty eyes.

METHODS: Patients with persistent PED who were treated with intravitreal aflibercept (2.0 mg) with ≥2 previous injections of bevacizumab (1.25 mg) or ranibizumab (0.5 mg) were analyzed.

RESULTS: Mean number of prior injections was 24.8 during a mean of 32 months of management (range 3 -77 months). Baseline mean PED height was 258 µm (range 80-687 µm), which decreased at 1, 6, and 12 months upon switching to aflibercept to 226 µm (-14%, range 34-701 µm), 215 µm (-18%, range 0-666 µm), and 208 µm (-22%, range 0-752 µm), respectively. The majority of eyes experienced a decrease in PED height after switching to aflibercept: 50/58 (86%), 38/47 (81%), and 37/47 (79%) at months 1, 6, and 12, respectively. Reduction in PED height was weakly correlated with improved visual acuity (R(2) = 0.11).

CONCLUSIONS: Intravitreal aflibercept resulted in significant reduction in PED height in previously treated eyes with neovascular AMD.

PMID: 26455973 [PubMed - in process]

Retina. 2015 Oct 9. [Epub ahead of print]

CHARACTERIZING THE EFFECT OF ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY ON TREATMENT-NAIVE CHOROIDAL NEOVASCULARIZATION USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY.

Muakkassa NW, Chin AT, de Carlo T, Klein KA, Baumal CR, Witkin AJ, Duker JS, Waheed NK.

PURPOSE: To use optical coherence tomography angiography (OCTA) to characterize the effects of anti-VEGF injections on treatment-naive choroidal neovascularization (CNV).

METHODS: From August 2014 to May 2015, treatment-naive eyes with CNV were scanned using a prototype OCTA system on a commercially available SD-OCT device (Optovue Inc, Fremont, CA). Optical coherence tomography angiography scans were obtained before anti-VEGF injection and at follow-up visits. The CNV area and greatest linear dimension (GLD) were measured along with the maximum retinal pigment epithelial detachment (RPED) height. Changes in subretinal and/or intraretinal fluid were also assessed.

RESULTS: Six eyes of six patients with treatment-naive CNV were included. Diagnoses included neovascular age-related macular degeneration, idiopathic polypoidal choroidal vasculopathy, CNV secondary to central serous chorioretinopathy and multifocal choroiditis, and macular telangiectasia Type 2 with subretinal neovascularization. After treatment, all patients with fluid on OCT initially showed a decrease in the amount of fluid. Five of six patients demonstrated decreases in CNV GLD and area with an average reduction of 23.6% and 29.8% respectively.

CONCLUSION: Both CNV greatest linear dimension and area measured using OCTA decreased after anti-VEGF treatment in most patients. Optical coherence tomography angiography may be a useful tool for monitoring and quantifying the response of CNV to treatment.

PMID: 26457400 [PubMed - as supplied by publisher]

Indian J Ophthalmol. 2015 Jul;63(7):616-8.

Intravitreal aflibercept for management of subfoveal choroidal neovascularization secondary to angioid streaks.

Esen E, Sizmaz S, Demircan N.

Abstract: In this study, we reported the clinical results of switching from ranibizumab to aflibercept for the treatment of an insufficient responder with choroidal neovascularization (CNV) secondary to angioid streaks (AS). A 39-year-old female patient with CNV secondary to AS had bilateral persistent intraretinal and subretinal fluid on the optical coherence tomography despite prior intravitreal 0.5 mg ranibizumab injections. The therapy was switched to intravitreal injection of aflibercept. The patient received a loading dose of three intravitreal 2 mg aflibercept injections at 4-week intervals for both eyes. Morphological and functional effects were observed as early as 1-week after the first injection. After the third aflibercept injection, her visual acuity improved, intraretinal and subretinal fluid resolved, and central macular thickness

reduced in both eyes. This is an early, but encouraging and promising result indicating that aflibercept might be a good alternative management for CNV secondary to AS that is insufficiently responding to prior ranibizumab injections.

PMID: 26458482 [PubMed - in process]

Curr Eye Res. 2015 Oct 15:1-6. [Epub ahead of print]

A Simple Spontaneous Vitreal Reflux Collecting Procedure During Intravitreal Injection: Set-Up and Validation Studies.

Cacciamani A, Parravano M, Scarinci F, Esposito G, Varano M, Micera A.

AIM: To set-up a simple technique for collecting spontaneous vitreal reflux (VR) in patients undergoing intravitreal injection. Both total protein concentration and vascular endothelial growth factor (VEGF)/ Interleukin 13 (IL13) levels were used to validate the technique.

METHODS: Sixty consecutive patients with neovascular age-related macular degeneration (nAMD, vitreal reflux drop, VR) and 10 patients underwent vitrectomy for macular hole (whole vitreous removal) were enrolled for the study as controls. Thirty-three out of 60 patients were also subjected to tear sampling. VR sampling was performed after the intravitreal injection. Four sampling tools (10 Schirmer strips, 10 microsponges, 20 millipore filters; 20 micropipettes) were tested. Analysis of protein concentration/ composition was performed between VR samples and vitreous samples to analyze the difference. The concentration of VEGF and IL 13 levels between cases and control samples were compared.

RESULTS: Millipore and micropipette techniques allowed the collection of higher protein concentrations in VR samples, comparison of both protein concentrations revealed no significant difference in the protein profile. However, the micropipette sampling was found easier to perform and did not require additional protein extraction from a solid support (membrane). Indeed, tear proteins and drug contaminants were not detected in micropipette samples. Increased VEGF levels were detected in naive VR group and to a less extend in VR group of nAMD patients undergoing intravitreal injection, with respect to the controls (macular holes). No significant differences in IL13 levels were quantified in nAMD sub-groups, as compared to naive and controls.

CONCLUSIONS: Overall, we provide evidence for a safe method for sampling VR at the end of intravitreal injection. This procedure might represent an interesting approach either for the prognosis of disease or monitoring the efficacy of intravitreal therapy.

PMID: 26470652 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2015 Oct 13. [Epub ahead of print]

[Unilateral Ranibizumab Treatment and Reduction of Macular Edema in the Contralateral Eye. Medication Effect or Natural Course?] [Article in German]

Girbardt C, Jochmann C, Wiedemann P.

Background: During unilateral treatment with ranibizumab, a reduction in the retinal thickness in the non-treated eye is occasionally observed. This may be due to the natural progression of the condition. It could also be the consequence of systemic absorption of intravitreal injections, leading to effects in the contralateral eye.

Patients: We describe 40 patients with either exsudative age-related macular degeneration (AMD) or diabetic macular oedema (DME). During treatment with ranibizumab, a reduction in retinal thickness in the contralateral eye was observed in this group (observation group). Another 40 AMD or diabetes patients under treatment with ranibizumab were selected as control group. These patients showed retinal swelling in the contralateral eye, which remained stable or increased.

Results: In the observation group, 58% of the patients had a DME and 42% had an AMD; in the control group, 25% of the patients had a DME and 75% of the patients had an AMD (p = 0.003). Retinal thickness before injection was 519 ± 126 µm in the observation group and 432 ± 87 µm in the control group (p = 0.003). Retinal thickness in the contralateral eye was then 511 ± 162 µm in the observation group and 436 ± 149 µm in the control group (p = 0.036). The reduction in retinal thickness in the injected eye was 214 ± 144 µm in the observation group and 150 ± 89 µm in the control group (p = 0.06).

Conclusion: In the group of patients that showed reduction in retinal thickness under ranibizumab in the contralateral eye, there were more diabetes patients than in the comparable control group. Even before injection, these patients showed higher retinal thickness in both eyes than did those in the control group. Further prospective studies would be required to confirm a possible causal connection between ranibizumab injection and reduction in DME in the contralateral eye.

PMID: 26460574 [PubMed - as supplied by publisher]

PLoS One. 2015 Oct 12;10(10):e0139556. eCollection 2015.

Treatment Options for Age-Related Macular Degeneration: A Budget Impact Analysis from the Perspective of the Brazilian Public Health System.

Elias FT, Silva EN, Belfort R Jr, Silva MT, Atallah ÁN.

BACKGROUND: Age-related macular degeneration (AMD) is a disease that causes reduced visual acuity and blindness. The new treatment options for AMD are not provided by the Brazilian public health system.

OBJECTIVE: To conduct a budget impact analysis of three scenarios for the introduction of AMD treatments: all the medications (verteporfin, ranibizumab, and bevacizumab-the reference scenario), ranibizumab alone, and bevacizumab alone.

METHODS: The basic assumption was that the Brazilian public health system would treat the entire target population with AMD aged > 70 years between 2008 and 2011. The size of the population of interest was estimated from official population projections and the prevalence of the disease was obtained from a systematic review. Medication prices were estimated by weighting their market values with correction factors to take account of the public procurement policy. The possibility of aliquoting bevacizumab was also considered. A panel of experts was consulted to estimate the market share of the different medications for the reference scenario. The incremental costs of the ranibizumab-alone and bevacizumab-alone scenarios compared to the reference scenario were calculated. Univariate sensitivity analyses were run to check the robustness of the model.

RESULTS: In four years, the Brazilian public health system would have treated 1,136,349 individuals with AMD. The annual costs of treating one patient would have been US$476.65 for bevacizumab, US$11,469.39 for ranibizumab, and US$4,376.28 for verteporfin. The incremental cost of the ranibizumab-alone scenario would have been US$1,878,318,056.00 in four years, while the incremental cost for the bevacizumab-alone scenario would have been a reduction of US$4,978,326,359.00 (i.e., a cost saving) in the same period. The bevacizumab-alone option was found to represent a cost saving across sensitivity analyses.

CONCLUSION: The introduction of bevacizumab for the treatment of AMD is recommended for the Brazilian Public Health System.

PMID: 26457416 [PubMed - in process]

Korean J Ophthalmol. 2015 Oct;29(5):315-24. Epub 2015 Sep 22.

Clinical Outcomes of Eyes with Submacular Hemorrhage Secondary to Age-related Macular Degeneration Treated with Anti-vascular Endothelial Growth Factor.

Kim KH, Kim JH, Chang YS, Lee TG, Kim JW, Lew YJ.

PURPOSE: To evaluate the long-term outcomes of intravitreal anti-vascular endothelial growth factor (VEGF) monotherapy for patients diagnosed with submacular hemorrhage secondary to exudative age-related macular degeneration.

METHODS: This retrospective, observational study included 49 patients (49 eyes) who initially presented with submacular hemorrhage associated with exudative age-related macular degeneration and who were followed-up for at least 24 months. Only eyes that were treated with intravitreal anti-VEGF monotherapy were included in the study. Best-corrected visual acuity (BCVA) measurements obtained at diagnosis, six months, and the final visit were compared. The associations of BCVA at the final visit with baseline BCVA, BCVA at six months, symptom duration, hemorrhage extent, and central foveal thickness were also analyzed.

RESULTS: Over the course of follow-up (mean, 32.1 ± 8.5 months), an average of 5.1 ± 2.2 anti-VEGF injections were administered. Recurrent hemorrhage was noted in 13 eyes (26.5%). The mean logarithm of the minimal angle of resolution BCVA at diagnosis, six months, and the final visit were 1.40 ± 0.52, 0.87 ± 0.64, and 1.03 ± 0.83, respectively. Both baseline BCVA ($p = 0.012$) and BCVA at six months ($p < 0.001$) were significantly associated with BCVA at the final visit.

CONCLUSIONS: Improved visual acuity was maintained for more than two years with intravitreal anti-VEGF monotherapy. BCVA at six months is a useful clinical index to predict long-term visual prognosis.

PMID: 26457037 [PubMed - in process] PMCID: PMC4595257

J Fr Ophtalmol. 2015 Oct 5. [Epub ahead of print]

[Comparison of early management of central retinal vein occlusion with ranibizumab versus hemodilution]. [Article in French]

Graber M, Glacet-Bernard A, Fardeau C, Massamba N, Atassi M, Rostaqui O, Coscas F, Le Hoang P, Souied EH.

PURPOSE: This study was designed to evaluate and compare the efficacy of early treatment of CRVO with either hemodilution by erythrocytopheresis or intravitreal (IVT) ranibizumab, or both.

MATERIAL AND METHODS: A multicentric prospective randomized study including patients with CRVO for less than 1 month was designed. Patients were randomized into 3 treatment groups: hemodilution (HD group), 3 monthly intravitreal injections of ranibizumab followed by PRN treatment (IVT group), or combined treatment (IVT+HD group). A monthly evaluation during a 6-month follow-up included best-corrected visual acuity (BCVA) and macular thickness measurements with OCT. Fluorescein angiography was performed at baseline, month 2 and month 6. Local and systemic tolerability of the different treatments were also compared.

RESULTS: Forty-four CRVO patients were included between February 2010 and June 2013: 20 in the IVT group, 13 in the HD group and 11 in the HD+IVT group. The mean duration of CRVO at baseline was 10 days and 16 days at the time of treatment without any significant difference between groups. Retinal ischemia was present at baseline in 40% of eyes in each group. After a 6-month follow-up, no difference between the 3 groups was observed in BCVA (10.5 ETDRS letters, 14.6 and 14.1 in the IVT group, HD group and IVT+HD group respectively, P=0.726) or in macular thickness (398µ, 440µ and 379µ respectively, P=0.465). The time until treatment from CRVO onset, ranging from 1 to 35 days, was not correlated to final outcomes. No significant difference in the mean number of IVT (3.2 in the IVT+HD group vs 3.7 in the IVT group) was observed at 6 months.

CONCLUSION: No difference in BCVA nor in macular thickness was seen at M6 between the study groups. The duration of CRVO at the time of the initiation of the treatment was not correlated to better visual outcomes. Therefore, etiologic treatment with HD can still be proposed as a first-line treatment in young patients, which allows delaying or avoiding the IVT treatment and its potential side effects. Anti-VEGF IVT still remains an effective option in every case and can be started one month after the beginning of the CRVO.

PMID: 26456487 [PubMed - as supplied by publisher]

Can J Ophthalmol. 2015 Oct;50(5):395.

Intravitreal ranibizumab for treatment of fibrovascular pigment epithelial detachment in age-related macular degeneration.

Yolcu U, Tas A, Altun S.

PMID: 26455979 [PubMed - in process]

Other treatment & diagnosis

Ophthalmic Surg Lasers Imaging Retina. 2015 Oct 1;46(9):907-12.

Optical Coherence Tomography Angiography Reveals Mature, Tangled Vascular Networks in Eyes With Neovascular Age-Related Macular Degeneration Showing Resistance to Geographic Atrophy.

Dansingani KK, Freund KB.

BACKGROUND AND OBJECTIVE: To demonstrate a vascular pattern seen on optical coherence tomography angiography (OCTA) that appears to correlate with reduced rates of geographic atrophy (GA) in eyes receiving long-term anti-vascular endothelial growth factor (VEGF) treatment for neovascular age-related macular degeneration (AMD).

PATIENTS AND METHODS: Non-consecutive, retrospective cohort study. Patients were included if they had received more than 50 anti-VEGF injections during a period of at least 4 years for neovascular AMD in at least one eye, with absence or minimal progression of GA. Clinical charts and imaging were reviewed retrospectively; study eyes underwent OCTA.

RESULTS: Nine eyes of eight patients were included. Mean age was 82 years, and mean follow-up of study eyes 9.1 years; study eyes received a mean of 65.8 injections. OCTA revealed tangled networks of neovessels associated with type 1 lesions.

CONCLUSION: With prolonged anti-VEGF treatment, GA appears to occur less commonly in eyes with type 1 neovascularization. OCTA shows mature tangled vessels with substantial flow within type 1 lesions. Mature, tangled networks may be associated with a decreased likelihood of developing GA despite the presence of choriocapillaris atrophy.

PMID: 26469229 [PubMed - in process]

Can J Ophthalmol. 2015 Oct;50(5):345-9.

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

Yau GL, Campbell RJ, Li C, Sharma S.

OBJECTIVE: To compare the peripapillary retinal nerve fibre layer (RNFL) thickness in nonexudative versus exudative age-related macular degeneration (wet AMD) eyes treated chronically with intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF).

DESIGN: Cross-sectional study.

PARTICIPANTS: Twenty-nine patients with unilateral wet AMD with at least 12 prior intravitreal anti-VEGF injections and 2 years of therapy were analyzed. The fellow eye with nonexudative (dry) AMD with no prior treatment served as the control group.

METHODS: All patients were prospectively enrolled from a single academic subspecialist practice. Bilateral spectral-domain optical coherence tomography (Cirrus SD-OCT; Carl Zeiss Meditec, Dublin, Calif.) of the peripapillary RNFL was performed on all pairs of eyes. Optic nerve head (ONH) parameters were also

computed. The primary outcome was mean difference in peripapillary RNFL thickness compared between the treated and the nontreated eyes.

RESULTS: Mean RNFL in the chronically treated eyes (95.0 [95% CI 89.8-100.2] μm) was significantly greater than the nontreated fellow eyes (89.9 [95% CI 85.5-94.3] μm) (p = 0.01). Quadrantic optic nerve analysis revealed the temporal RNFL to be greater in the treated group (p = 0.02), whereas all other locations were similar. No significant differences were found between the 2 groups in any ONH parameters.

CONCLUSIONS: This study demonstrated no deleterious optic nerve RNFL thinning in a series of wet AMD eyes with long-term repetitive exposure to intravitreal anti-VEGF injections. Furthermore, we observed that those with wet AMD have a relatively thickened temporal peripapillary RNFL layer, which is an important association for all observers of optic nerve disease.

PMID: 26455968 [PubMed - in process]

JAMA Ophthalmol. 2015 Oct 15:1-6. [Epub ahead of print]

Qualifying to Use a Home Monitoring Device for Detection of Neovascular Age-Related Macular Degeneration.

Thomas M, Wolfson Y, Zayit-Soudry S, Bressler SB, Bressler NM.

IMPORTANCE: Patients with intermediate age-related macular degeneration (AMD) using a home monitoring device have less loss of visual acuity, on average, at detection of choroidal neovascularization than do individuals using standard care monitoring techniques. Understanding the frequency with which patients are likely to initiate using a home monitoring device successfully is important in planning implementation of the device into practice.

OBJECTIVES: To determine the frequency with which patients with intermediate AMD qualify to use a home monitoring device and to establish a reliable baseline reference value with the device to monitor their AMD for progression to choroidal neovascularization.

DESIGN, SETTING, AND PARTICIPANTS: Between October 8, 2010, and May 20, 2011, a total of 131 eligible participants within a university-based retina practice with intermediate AMD in the study eye and visual acuity of 20/63 or better completed an in-clinic qualification test for the home device. Intermediate AMD was defined as multiple intermediate-sized drusen or at least 1 large druse. If both eyes were eligible, the eye with better visual acuity was selected as the study eye. If both eyes had the same visual acuity, the patient used the eye with subjectively better vision. Analysis was performed between August 1, 2011, and January 11, 2014.

MAIN OUTCOMES AND MEASURES: The proportion of patients with reliable qualification test results and a test score predictive of successful home use of a monitoring device for detecting neovascular AMD, and the proportion who established a baseline reference value at home.

RESULTS: A total of 129 participants (98.5%; 95% CI, 96.4%-99.9%) had reliable qualification test results; 91 participants (69.5%; 95% CI, 61.6%-77.4%) who completed this test attained a score that suggested they would be able to successfully use the home device. Among the 91 participants who could initiate home testing, 83 did so, including 80 participants (87.9%; 95% CI, 81.2%-94.6%) who established a baseline value that could be used as a reference for future monitoring. Younger participants were more likely to qualify for home testing (mean [SD] age, 73.1 [8.4] vs 81.1 [7.1] years; P < .001). Visual acuity at study enrollment did not appear to be associated with successful qualification (mean visual acuity for those who did and did not qualify was 20/28 and 20/31, respectively; P = .10).

CONCLUSIONS AND RELEVANCE: These data suggest that the in-office qualification test is a useful screening tool to identify patients who may benefit from the home device. In any given retina practice, our data suggest an estimated 61.6% to 77.4% of patients with intermediate AMD should be able to produce reliable initial test results in the office test using the home monitoring device and pass a qualification test to initiate home monitoring. Subsequently, 81.2% to 94.6% of patients should be able to establish a home baseline reference value for future monitoring.

PMID: 26468999 [PubMed - as supplied by publisher]

Clin Experiment Ophthalmol. 2015 Oct 15. [Epub ahead of print]

Prognostic implications of imaging in atrophic macular degeneration and its use in clinical practice and clinical trial design.

Lim PC, Layton CJ.

Abstract: Clinical prognostic markers in atrophic age-related macular degeneration (AMD) include the extent of existing atrophy, fundus autofluorescence (FAF) patterns and optical coherence tomography (OCT) changes in the outer retina/retinal pigment epithelium (RPE) interface. The prognostic implications of these findings may be used to determine not just the rate of disease progression but also influence the likelihood, magnitude and clinical relevance of therapy responses. FAF phenotypes have been extensively investigated, however, the pathophysiological mechanisms behind their appearance has not been fully elucidated. OCT imaging is additive to FAF imaging in atrophic AMD, allowing the visualisation of detail not available through FAF imaging whilst also displaying subtle changes correlating with the FAF phenotypes themselves, thereby giving clues to their histological determinates. The developing understanding of these imaging modalities and consequent development of prognostically useful classification systems have widespread implication in clinical care and clinical trial design. This paper examines the evidence for the existence of the FAF phenotypes and their potential usefulness in clinical practice and scientific ophthalmology.

PMID: 26468964 [PubMed - as supplied by publisher]

Retina. 2015 Oct 9. [Epub ahead of print]

OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN EARLY TYPE 3 NEOVASCULARIZATION.

Miere A, Querques G, Semoun O, El Ameen A, Capuano V, Souied EH.

PURPOSE: To report the imaging features of Type 3 neovascularization secondary to exudative age-related macular degeneration on optical coherence tomography angiography (OCTA).

METHODS: All consecutive treatment-naive patients diagnosed with early-stage Type 3 neovascularization underwent imaging by color retinal photographs or multicolor imaging, fluorescein angiography, indocyanine green angiography, spectral domain optical coherence tomography, and OCTA. The OCTA features were analyzed and correlated with the findings of conventional angiography and spectral domain optical coherence tomography.

RESULTS: A total of 18 treatment-naive eyes of 18 consecutive patients (13 females and 5 males; mean age 81.3 ± 6.0) were included in the analysis. Optical coherence tomography angiography showed lesions characterized by a retinal-retinal anastomosis that emerged from the deep capillary plexus, forming in all 18 eyes a clear tuft-shaped high-flow network in the outer retinal segmentation, finally abutting in the subretinal pigment epithelium space. In 15 of 18 eyes, in the choriocapillaris segmentation, there appeared a small clew-like lesion, which in 2 cases seemed connected with the choroid through a small caliber vessel.

CONCLUSION: Optical coherence tomography angiography of treatment-naive Type 3 neovascularization showed almost constantly a high-flow, tuft-shaped abnormal outer retinal proliferation, frequently associated to a small clew-like lesion in the choriocapillaris layer.

PMID: 26457399 [PubMed - as supplied by publisher]

Retina. 2015 Oct 9. [Epub ahead of print]

OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY FEATURES OF SUBRETINAL FIBROSIS IN AGE-RELATED MACULAR DEGENERATION.

Miere A, Semoun O, Cohen SY, El Ameen A, Srour M, Jung C, Oubraham H, Querques G, Souied EH.

PURPOSE: To report the imaging features of subretinal fibrosis secondary to exudative age-related

macular degeneration (AMD) on optical coherence tomography angiography.

METHODS: All consecutive patients diagnosed with subretinal fibrosis complicating exudative AMD were imaged by color retinal photographs or multicolor imaging, fluorescein angiography, spectral domain optical coherence tomography, and optical coherence tomography angiography. Eyes with active exudative features observed during the last 6 months were compared with those without any sign of exudation >6 months.

RESULTS: Forty-nine eyes of 47 consecutive patients were included. A blood flow inside the fibrotic scar could be detected in 46 of 49 cases (93.8%). Three patterns of vascular networks could be distinguished, that were described as pruned vascular tree (26 of 49 eyes; 53.1%), tangled network (14 of 49; 28.6%), and/or vascular loop (25 of 49; 51.0%). Furthermore, 2 types of hyporeflective structures, large flow void, and/or dark halo were observed in 63% and in 65% of eyes, respectively. The observed patterns did not differ between eyes with active or inactive lesions.

CONCLUSION: Optical coherence tomography angiography of subretinal fibrosis showed almost constantly a perfused, abnormal vascular network and collateral architectural changes in the outer retina and the choriocapillaris layer. These features were associated with both active and inactive fibrotic choroidal neovessels.

PMID: 26457397 [PubMed - as supplied by publisher]

J Cataract Refract Surg. 2015 Oct 12. [Epub ahead of print]

Prevention of increased abnormal fundus autofluorescence with blue light-filtering intraocular lenses.

Nagai H, Hirano Y, Yasukawa T, Morita H, Nozaki M, Wolf-Schnurrbusch U, Wolf S, Ogura Y.

PURPOSE: To observe changes in fundus autofluorescence 2 years after implantation of blue light-filtering (yellow-tinted) and ultraviolet light-filtering (colorless) intraocular lenses (IOLs).

SETTING: Department of Ophthalmology and Visual Science, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, and the Department of Ophthalmology, University of Bern, Bern, Switzerland.

DESIGN: Prospective comparative observational study.

METHODS: Patients were enrolled who had cataract surgery with implantation of a yellow-tinted or colorless IOL and for whom images were obtained on which the fundus autofluorescence was measurable using the Heidelberg Retina Angiogram 2 postoperatively. The fundus autofluorescence in the images was classified into 8 abnormal patterns based on the classification of the International Fundus Autofluorescence Classification Group, The presence of normal fundus autofluorescence, geographic atrophy, and wet age-related macular degeneration (AMD) also was recorded. The fundus findings at baseline and 2 years postoperatively were compared.

RESULTS: Fifty-two eyes with a yellow-tinted IOL and 79 eyes with a colorless IOL were included. Abnormal fundus autofluorescence did not develop or increase in the yellow-tinted IOL group; however, progressive abnormal fundus autofluorescence developed or increased in 12 eyes (15.2%) in the colorless IOL group (P = .0016). New drusen, geographic atrophy, and choroidal neovascularization were observed mainly in the colorless IOL group. The incidence of AMD was statistically significantly higher in the colorless IOL group (P = .042).

CONCLUSIONS: Two years after cataract surgery, significant differences were seen in the progression of abnormal fundus autofluorescence between the 2 groups. The incidence of AMD was lower in eyes with a yellow-tinted IOL.

PMID: 26471051 [PubMed - as supplied by publisher]

IEEE J Biomed Health Inform. 2015 Oct 14. [Epub ahead of print]

Retinal Disease Screening through Local Binary Patterns.

Morales S, Engan K, Naranjo V, Colomer A.

Abstract: This work investigates discrimination capabilities in the texture of fundus images to differentiate between pathological and healthy images. For this purpose, the performance of Local Binary Patterns (LBP) as a texture descriptor for retinal images has been explored and compared with other descriptors such as LBP filtering (LBPF) and local phase quantization (LPQ). The goal is to distinguish between diabetic retinopathy (DR), agerelated macular degeneration (AMD) and normal fundus images analysing the texture of the retina background and avoiding a previous lesion segmentation stage. Five experiments (separating DR from normal, AMD from normal, pathological from normal, DR from AMD and the three different classes) were designed and validated with the proposed procedure obtaining promising results. For each experiment, several classifiers were tested. An average sensitivity and specificity higher than 0.86 in all the cases and almost of 1 and 0.99, respectively, for AMD detection were achieved. These results suggest that the method presented in this paper is a robust algorithm for describing retina texture and can be useful in a diagnosis aid system for retinal disease screening.

PMID: 26469792 [PubMed - as supplied by publisher]

Retina. 2015 Oct 14. [Epub ahead of print]

DETECTION OF NONEXUDATIVE CHOROIDAL NEOVASCULARIZATION IN AGE-RELATED MACULAR DEGENERATION WITH OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY.

Palejwala NV, Jia Y, Gao SS, Liu L, Flaxel CJ, Hwang TS, Lauer AK, Wilson DJ, Huang D, Bailey ST.

PURPOSE: To evaluate eyes with age-related macular degeneration and high-risk characteristics for choroidal neovascularization (CNV) with optical coherence tomographic (OCT) angiography to determine whether earlier detection of CNV is possible.

METHODS: Eyes with drusen, pigmentary changes, and with CNV in the fellow eye were scanned with a 70-kHz spectral domain OCT system (Optovue RTVue-XR Avanti). The split-spectrum amplitude-decorrelation angiography (SSADA) algorithm was used to distinguish blood flow from static tissue. Two masked graders reviewed scans for CNV, defined as flow in the outer retinal/sub-RPE slab. Choroidal neovascularization flow area repeatability and between-grader reproducibility were calculated.

RESULTS: Of 32 eyes, 2 (6%) were found to have Type 1 CNV with OCT angiography. The lesions were not associated with leakage on fluorescein angiography or fluid on OCT. One case was followed for 8 months without treatment, and the CNV flow area enlarged slightly without fluid buildup on OCT or vision loss. Between-grader reproducibility of the CNV flow area was 9.4% (coefficient of variation) and within-visit repeatability was 5.2% (pooled coefficient of variation).

CONCLUSION: Optical coherence tomographic angiography can detect the presence of nonexudative CNV, lesions difficult to identify with fluorescein angiography and OCT. Further study is needed to understand the significance and natural history of these lesions.

PMID: 26469533 [PubMed - as supplied by publisher]

Indian J Ophthalmol. 2015 Jul;63(7):575-81.

Update on wide- and ultra-widefield retinal imaging.

Shoughy SS, Arevalo JF, Kozak I.

Abstract: The peripheral retina is the site of pathology in many ocular diseases and ultra-widefield (UWF) imaging is one of the new technologies available to ophthalmologists to manage some of these diseases.

Currently, there are several imaging systems used in practice for the purpose of diagnostic, monitoring disease progression or response to therapy, and telemedicine. These include modalities for both adults and pediatric patients. The current systems are capable of producing wide- and UWF color fundus photographs, fluorescein and indocyanine green angiograms, and autofluorescence images. Using this technology, important clinical observations have been made in diseases such as diabetic retinopathy, uveitides, retinal vascular occlusions and tumors, intraocular tumors, retinopathy of prematurity, and age-related macular degeneration. Widefield imaging offers excellent postoperative documentation of retinal detachment surgery. New applications will soon be available to integrate this technology into large volume routine clinical practice.

PMID: 26458474 [PubMed - in process]

Am J Ophthalmol. 2015 Oct 9. [Epub ahead of print]

Macular Ganglion Cell Complex and Retinal Nerve Fiber Layer Comparison in Different Stages of Age-Related Macular Degeneration.

Zucchiatti I, Parodi MB, Pierro L, Cicinelli MV, Gagliardi M, Castellino N, Bandello F.

PMID: 26459982 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2015 Oct 9. [Epub ahead of print]

Macular Ganglion Cell Complex and Retinal Nerve Fiber Layer Comparison in Different Stages of Age-Related Macular Degeneration.

Lee HJ, Kim MS, Jo YJ, Kim JY.

PMID: 26459981 [PubMed - as supplied by publisher]

Pathogenesis

Sci Transl Med. 2015 Oct 14;7(309):309ra165.

The peptidomimetic Vasotide targets two retinal VEGF receptors and reduces pathological angiogenesis in murine and nonhuman primate models of retinal disease.

Sidman RL, Li J, Lawrence M, Hu W, Musso GF, Giordano RJ, Cardó-Vila M, Pasqualini R, Arap W.

Abstract: Blood vessel growth from preexisting vessels (angiogenesis) underlies many severe diseases including major blinding retinal diseases such as retinopathy of prematurity (ROP) and aged macular degeneration (AMD). This observation has driven development of antibody inhibitors that block a central factor in AMD, vascular endothelial growth factor (VEGF), from binding to its receptors VEGFR-1 and mainly VEGFR-2. However, some patients are insensitive to current anti-VEGF drugs or develop resistance, and the required repeated intravitreal injection of these large molecules is costly and clinically problematic. We have evaluated a small cyclic retro-inverted peptidomimetic, D(Cys-Leu-Pro-Arg-Cys) [D (CLPRC)], and hereafter named Vasotide, that inhibits retinal angiogenesis by binding selectively to the VEGF receptors VEGFR-1 and neuropilin-1 (NRP-1). Delivery of Vasotide via either eye drops or intraperitoneal injection in a laser-induced monkey model of human wet AMD, a mouse genetic knockout model of the AMD subtype called retinal angiomatous proliferation (RAP), and a mouse oxygen-induced model of ROP decreased retinal angiogenesis in all three animal models. This prototype drug candidate is a promising new dual receptor inhibitor of the VEGF ligand with potential for translation into safer, less-invasive applications to combat pathological angiogenesis in retinal disorders.

PMID: 26468327 [PubMed - in process]

J Biol Chem. 2015 Oct 14. [Epub ahead of print]

A2E Accumulation and the Maintenance of the Visual Cycle are Independent of Atg7-mediated Autophagy in the Retinal Pigmented Epithelium.

Perusek L, Sahu B, Parmar T, Maeno H, Arai E, Le YZ, Subauste CS, Chen Y, Palczewski K, Maeda A.

Abstract: Autophagy is an evolutionarily conserved catabolic mechanism that relieves cellular stress by removing/recycling damaged organelles and debris through the action of lysosomes. Compromised autophagy has been implicated in many neurodegenerative diseases, including retinal degeneration. Here we examined retinal phenotypes resulting from RPE-specific deletion of the autophagy regulatory gene Atg7 by generating Atg7flox/flox;VMD2-rtTA-cre+ mice to determine whether autophagy is essential for RPE functions including retinoid recycling. Atg7 deficient RPE displayed abnormal morphology with increased RPE thickness, cellular debris and vacuole formation indicating that autophagy is important in maintaining RPE homeostasis. In contrast, 11-cis-retinal content, ERGs and retinal histology were normal in mice with Atg7 deficient RPE in both fasted and fed states. Because A2E accumulation in the RPE is associated with pathogenesis of both Stargardt disease and age-related macular degeneration (AMD) in humans, deletion of Abca4 was introduced into Atg7flox/flox;VMD2-rtTA-cre+ mice to investigate the role of autophagy during A2E deposition. Comparable A2E concentrations were detected in the eyes of 6-month-old mice with and without Atg7 from both Abca4-/- and Abca4+/+ backgrounds. To identify other autophagy-related molecules involved in A2E accumulation, we performed gene expression array analysis on A2E-treated human RPE cells and found upregulation of four autophagy related genes; DRAM1, NPC1, CASP3, and EIF2AK3/PERK. These observations indicate that Atg7-mediated autophagy is dispensable for retinoid recycling and A2E deposition; however, autophagy plays a role in coping with stress caused by A2E accumulation.

PMID: 26468292 [PubMed - as supplied by publisher]

Neurosci Lett. 2015 Oct 11. [Epub ahead of print]

Unfolded Protein Response is Activated in Aged Retinas.

Lenox AR, Bhootada Y, Gorbatyuk O, Fullard R, Gorbatyuk M.

Abstract: An unfolded protein response (UPR) in addition to oxidative stress and the inflammatory response is known to be activated in age-related ocular disorders, such as macular degeneration, diabetic retinopathy, glaucoma, and cataracts. Therefore, we aimed to investigate whether healthy aged retinas display UPR hallmarks, in order to establish a baseline for the activated UPR markers for age-related ocular diseases. Using western blotting, we determined that the hallmarks of the UPR PERK arm, phosphorylated (p) eIF2a, ATF4, and GADD34, were significantly altered in aged vs. young rat retinas. The cleaved pATF6 (50) and CHOP proteins were dramatically upregulated in the aged rodent retinas, indicating the activation of the ATF6 UPR arm. The UPR activation was associated with a drop in rhodopsin expression and in the NRF2 and HO1 levels, suggesting a decline in the anti-oxidant defense in aged retinas. Moreover, we observed down-regulation of anti-inflammatory IL-10 and IL-13 and upregulation of pro-inflammatory RANTES in the healthy aged retinas, as measured using the Bio-plex assay. Our results suggest that cellular homeostasis in normal aged retinas is compromised, resulting in the concomitant activation of the UPR, oxidative stress, and inflammatory signaling. This knowledge brings us closer to understanding the cellular mechanisms of the age-related retinopathies and ocular disorders characterized by an ongoing UPR, and highlight the UPR signaling molecules that should be validated as potential therapeutic targets.

PMID: 26467812 [PubMed - as supplied by publisher]

Am J Pathol. 2015 Oct 14. [Epub ahead of print]

Rap1 GTPase Inhibits Tumor Necrosis Factor-α-Induced Choroidal Endothelial Migration via NADPH

Oxidase- and NF-κB-Dependent Activation of Rac1.

Wang H, Fotheringham L, Wittchen ES, Hartnett ME.

Abstract: Macrophage-derived tumor necrosis factor (TNF)-α has been found in choroidal neovascularization (CNV) surgically removed from patients with age-related macular degeneration. However, the role of TNF-α in CNV development remains unclear. In a murine laser-induced CNV model, compared with un-lasered controls, TNF-α mRNA was increased in retinal pigment epithelial and choroidal tissue, and TNF-α colocalized with lectin-stained migrating choroidal endothelial cells (CECs). Inhibition of TNF-α with a neutralizing antibody reduced CNV volume and reactive oxygen species (ROS) level around CNV. In CECs, pretreatment with the antioxidant apocynin or knockdown of p22phox, a subunit of NADPH oxidase, inhibited TNF-α-induced ROS generation. Apocynin reduced TNF-α-induced NF-κB and Rac1 activation, and inhibited TNF-α-induced CEC migration. TNF-α-induced Rac1 activation and CEC migration were inhibited by NF-κB inhibitor Bay11-7082. Overexpression of Rap1a prevented TNF-α-induced ROS generation and reduced NF-κB and Rac1 activation. Activation of Rap1 by 8-(4-chlorophenylthio)adenosine -2'-O-Me-cAMP prevented TNF-α-induced CEC migration and reduced laser-induced CNV volume, ROS generation, and activation of NF-κB and Rac1. These findings provide evidence that active Rap1a inhibits TNF-α-induced CEC migration by inhibiting NADPH oxidase-dependent NF-κB and Rac1 activation and suggests that Rap1a de-escalates CNV development by interfering with ROS-dependent signaling in several steps of the pathogenic process.

PMID: 26476350 [PubMed - as supplied by publisher]

Genetics

BMC Bioinformatics. 2015 Oct 14;16(1):329.

Estimating cumulative pathway effects on risk for age-related macular degeneration using mixed linear models.

Hall JB, Cooke Bailey JN, Hoffman JD, Pericak-Vance MA, Scott WK, Kovach JL, Schwartz SG, Agarwal A, Brantley MA Jr, Haines JL, Bush WS.

BACKGROUND: Age-related macular degeneration (AMD) is the leading cause of irreversible visual loss in the elderly in developed countries and typically affects more than 10 % of individuals over age 80. AMD has a large genetic component, with heritability estimated to be between 45 % and 70 %. Numerous variants have been identified and implicate various molecular mechanisms and pathways for AMD pathogenesis but those variants only explain a portion of AMD's heritability. The goal of our study was to estimate the cumulative genetic contribution of common variants on AMD risk for multiple pathways related to the etiology of AMD, including angiogenesis, antioxidant activity, apoptotic signaling, complement activation, inflammatory response, response to nicotine, oxidative phosphorylation, and the tricarboxylic acid cycle. While these mechanisms have been associated with AMD in literature, the overall extent of the contribution to AMD risk for each is unknown.

METHODS: In a case-control dataset with 1,813 individuals genotyped for over 600,000 SNPs we used Genome-wide Complex Trait Analysis (GCTA) to estimate the proportion of AMD risk explained by SNPs in genes associated with each pathway. SNPs within a 50 kb region flanking each gene were also assessed, as well as more distant, putatively regulatory SNPs, based on DNaseI hypersensitivity data from ocular tissue in the ENCODE project.

RESULTS: We found that 19 previously associated AMD risk SNPs contributed to 13.3 % of the risk for AMD in our dataset, while the remaining genotyped SNPs contributed to 36.7 % of AMD risk. Adjusting for the 19 risk SNPs, the complement activation and inflammatory response pathways still explained a statistically significant proportion of additional risk for AMD (9.8 % and 17.9 %, respectively), with other pathways showing no significant effects (0.3 % - 4.4 %).

DISCUSSION: Our results show that SNPs associated with complement activation and inflammation significantly contribute to AMD risk, separately from the risk explained by the 19 known risk SNPs. We

found that SNPs within 50 kb regions flanking genes explained additional risk beyond genic SNPs, suggesting a potential regulatory role, but that more distant SNPs explained less than 0.5 % additional risk for each pathway.

CONCLUSIONS: From these analyses we find that the impact of complement SNPs on risk for AMD extends beyond the established genome-wide significant SNPs.

PMID: 26467978 [PubMed - in process]

Arq Bras Oftalmol. 2015 Oct;78(5):290-4.

Influence of VEGF-C936T genetic variant on age-related macular degeneration.

Gonçalves FT, Cezario SM, Calastri MC, Oliveira CI, Souza DR, Pinhel MA, Cotrim CC, Jorge R, Siqueira RC.

PURPOSE: To evaluate the association between the VEGF-C936T polymorphism and serum vascular endothelial growth factor (VEGF) levels, lifestyle, and demographic parameters in patients with age-related macular degeneration (AMD).

METHODS: A total of 183 individuals were enrolled in the present study, including 88 patients with AMD receiving clinical and pharmacological treatment (study group, SG) and 95 individuals without AMD as controls (control group, CG). The presence of the VEGF-C936T polymorphism and serum VEGF levels were determined using polymerase chain reaction/restriction fragment length polymorphism and enzyme-linked immunosorbent assay, respectively. Significance was set at $P<0.05$ for all statistical analyses.

RESULTS: The homozygous wild-type genotype (CC) and the C allele were predominant in both groups ($P=0.934$ and $P=0.938$, respectively). Serum VEGF levels (assessed in 57% and 31% of patients in the SG and CG, respectively) were comparable between groups (SG, 307.9 ± 223.6 pg/mL; CG, 305.1 ± 212.3 pg/mL; $P=0.955$). A significantly higher prevalence of smoking (44% vs 25%; $P=0.01$) and hypertension (66% vs 48%; $P=0.025$) was observed in the SG than in the CG. The distribution of alcohol consumption and dyslipidemia was similar between groups ($P>0.05$).

CONCLUSIONS: In the present study group of Brazilian patients, the VEGF-C936T polymorphism was not found to be associated with age-related macular degeneration. However, smoking and systemic arterial hypertension (SAH) were found to be potential independent risk factors for the development of age-related macular degeneration. Comparable serum VEGF levels in both study groups may reflect the efficacy of pharmacological treatment of AMD.

PMID: 26466227 [PubMed - in process]

Int J Clin Exp Pathol. 2015 Aug 1;8(8):9592-6. eCollection 2015.

CX3CR1 polymorphisms and the risk of age-related macular degeneration.

Ma B, Dang G, Yang S, Duan L, Zhang Y.

BACKGROUND: Age-related macular degeneration (AMD), a most common eye disease, can lead to irreversible visual impairment. Age, genetic and environmental factors have been implicated in AMD. Chemokine (C-X3-C motif) receptor 1 (CX3CR1) gene polymorphisms could influence the susceptibility of AMD.

METHODS: We tested the association between AMD and single nocleotide polymorphisms (SNPs) of CX3CR1 gene (rs3732378 and rs3732379) in 102 cases and 115 controls from China. Genotypes were determined by MassArray genotyping assay method. Association between CX3CR1 gene polymorphisms and AMD were examined by $\chi(2)$ test and logistic regression.

RESULTS: Genotype distribution of CX3CR1 gene polymorphisms were in accordance with HWE

examination. No obvious differences were observed in the genotypes of rs3732378 polymorphism between case and control groups (P>0.05), but A allele of it could increase the risk of AMD (P=0.025, OR=2.391, 95% CI=1.092-5.237). Both TT genotype and T allele of rs3732379 were significantly associated with the susceptibility of AMD (P=8.663, OR=8.663, 95% CI=1.044-71.874; P=0.021, OR=2.076, 95% CI=1.104-3.903). Age, gender and smoking status were used as common confounders to adjust the association between CX3CR1 gene polymorphism and AMD risk. Then we found that rs3732378 had no obvious association with AMD susceptibility. TT genotype of rs3732379 related to the occurrence of AMD, but the association was not significant (P=0.050, OR=8.274, 95% CI=1.002-69.963). T allele of rs3732379 might increase the susceptibility of AMD (P=0.029, OR=2.033, 95% CI=1.077-3.838).

CONCLUSION: T allele of rs3732379 might have a positive association with the susceptibility of AMD.

PMID: 26464724 [PubMed - in process]

Diet, lifestyle & low vision

Appl Biochem Biotechnol. 2015 Oct 14. [Epub ahead of print]

Amyloid β Peptide Induces Apoptosis Through P2X7 Cell Death Receptor in Retinal Cells: Modulation by Marine Omega-3 Fatty Acid DHA and EPA.

Wakx A, Dutot M, Massicot F, Mascarelli F, Limb GA, Rat P.

Abstract: Retinal Müller glial cells have already been implicated in age-related macular degeneration (AMD). AMD is characterized by accumulation of toxic amyloid-β peptide (Aβ); the question we raise is as follows: is P2X7 receptor, known to play an important role in several degenerative diseases, involved in Aβ toxicity on Müller cells? Retinal Müller glial cells were incubated with Aβ for 48 h. Cell viability was assessed using the alamarBlue assay and cytotoxicity using the lactate dehydrogenase (LDH) release assay. P2X7 receptor expression was highlighted by immunolabeling observed on confocal microscopy and its activation was evaluated by YO-PRO-1 assay. Hoechst 33342 was used to evaluate chromatin condensation, and caspases 8 and 3 activation was assessed using AMC assays. Lipid formulation rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) used in Age-Related Eye Disease Study 2 was incubated on cells for 15 min prior to Aβ incubation. For the first time, we showed that Aβ induced caspase-independent apoptosis through P2X7 receptor activation on our retinal model. DHA and EPA are polyunsaturated fatty acids recommended in food supplement to prevent AMD. We therefore modulated Aβ cytotoxicity using a lipid formulation rich in DHA and EPA to have a better understanding of the results observed in clinical studies. We showed that fish oil rich in EPA and DHA, in combination with a potent P2X7 receptor antagonist, represents an efficient modulator of Aβ toxicity and that P2X7 could be an interesting therapeutic target to prevent AMD.

PMID: 26467741 [PubMed - as supplied by publisher]

Exp Eye Res. 2015 Oct 14. [Epub ahead of print]

Berberine protects against light-induced photoreceptor degeneration in the mouse retina.

Song D, Song J, Wang C, Li Y, Dunaief JL.

Abstract: Oxidative stress and inflammation play key roles in the light damage (LD) model of photoreceptor degeneration, as well as in age-related macular degeneration (AMD). We sought to investigate whether Berberine (BBR), an antioxidant herb extract, would protect the retina against light-induced degeneration. To accomplish this, Balb/c mice were treated with BBR or PBS via gavage for 7 days, and then were placed in constant cool white light-emitting diode (LED) light (10,000 lux) for 4 hours. Retinal function and degeneration were evaluated by histology, electroretinography (ERG) and optical coherence tomography (OCT) at 7d after LD. Additionally, mRNA levels of cell-type specific, antioxidant, and inflammatory genes were compared 7d after LD. Photoreceptor DNA fragmentation was assessed via the terminal deoxynucleotidyl transferase dUTP nick end-labeling (TUNEL) assay. LD resulted in substantial

photoreceptor-specific cell death. Histological analysis using plastic sections showed dosing with BBR preserved photoreceptors. The ERG analysis demonstrated functional protection by BBR in rod-b, -a, and cone-b waves. In OCT images, mice receiving PBS showed severe thinning and disorganization of the photoreceptor layer 7 days after LD, whereas mice treated with BBR had significantly less thinning and disorganization. Consistent with OCT results, the mRNA levels of Rho in the NSR, and Rpe65 and Mct3 in the RPE, were significantly higher in mice treated with BBR. The numbers of TUNEL-positive photoreceptors were significantly decreased in BBR-treated mice. The retinal mRNA levels of oxidative stress genes, the number of microglia/macrophages, and the malondialdehyde (MDA) immunolabeling were significantly lower in BBR-treated mice compared to controls 48h after LD, which indicates oxidative stress was reduced by BBR in light-damaged eyes. In conclusion, systemic BBR is protective against light-induced retinal degeneration associated with diminished oxidative stress in the retina. These results suggest that BBR may be protective against retinal diseases involving oxidative stress.

PMID: 26475979 [PubMed - as supplied by publisher]

Qual Life Res. 2015 Oct 1. [Epub ahead of print]

Generic and disease-specific estimates of quality of life in macular degeneration: mapping the MacDQoL onto the EQ-5D-3L.

Dixon P, Dakin H, Wordsworth S.

PURPOSE: The macular degeneration quality of life (MacDQoL) instrument is a validated condition-specific measure of quality of life in patients with macular degeneration. This paper presents the first mapping algorithm to predict EQ-5D from responses to the MacDQoL instrument.

METHODS: Responses to the MacDQoL and EQ-5D-3L instruments from 482 patients were collected from the IVAN multicentre trial of two alternative drug treatments for neovascular age-related macular degeneration. Regression specifications were estimated using OLS, censored least absolute deviation, Tobit and two-part models. Their predictive performance was assessed using mean squared error. An internal validation sample based on a random selection of 25 % of patients was used to assess the performance of the model estimated on the remaining 75 % of patients.

RESULTS: A two-part model had the best predictive performance on the full sample. The covariates of this model include responses and weighted impact scores for all 23 condition-specific domains of the MacDQoL, and responses to a general MacDQoL quality of life question. The selected models were successful at predicting means and standard deviations of target populations, but prediction is weaker at the upper and lower extremes of the EQ-5D-3L distribution.

CONCLUSION: The mapping algorithms provide a means of predicting EQ-5D-3L index scores from MacDQoL scores, and could facilitate cost-effectiveness analyses when the latter but not the former are available to researchers. Further validation of the performance of the algorithms using external data would provide a means of establishing the robustness of the algorithms.

PMID: 26462812 [PubMed - as supplied by publisher]

Can J Ophthalmol. 2015 Oct;50(5):388-92.

A survey for the need of translational aids among Canadian ophthalmologists.

Mednick ZD, Cao K, Braga-Mele R.

OBJECTIVE: To conduct a needs assessment survey of Canadian ophthalmologists to determine whether there is a requirement for translational aids in ophthalmology, and if so, the content, format, and languages to include.

DESIGN: Anonymous voluntary online needs assessment questionnaire.

PARTICIPANTS: A total of 139 ophthalmologists completed the online needs assessment questionnaire.

METHODS: An anonymous voluntary online survey in English and French was distributed to 700 active members (practicing Canadian ophthalmologists) of the Canadian Ophthalmological Society. Data were collected regarding the potential utility of translational aids, as well as the contents and languages that should be included if such aids were to be created. Level of support for translational aids, as well as the contents and languages of potential translational aids, was assessed.

RESULTS: The survey response rate was 19.9% (139/700). The majority of the respondents (130/139, 93.5%) have encountered difficulty in communicating with patients because of language barrier, and 88.5% (123/139) would benefit from having a list of ophthalmologic terms translated into several of Canada's most popular languages. The top 10 languages that the respondents indicated would be most beneficial are (in descending order): Chinese, Hindi, Spanish, Punjabi, Italian, Portuguese, Arabic, Greek, Cree, and Vietnamese. The survey responses provided a comprehensive list of the most useful ophthalmologic symptoms, instructions to patients, and diagnoses to be translated. Most respondents (120/139, 86.3%) believed that having basic information pamphlets on specific ocular conditions translated into several languages would benefit their practice; the top 3 conditions were cataract, glaucoma, and age-related macular degeneration. Producing the translational aids in both paper and electronic format was found to be the most favoured (89/139, 64.0%).

CONCLUSIONS: Canadian ophthalmologists believe they would benefit from translational aids. The results of this survey provide a framework for the creation of such aids.

PMID: 26455976 [PubMed - in process]