Macular Disease Foundation AUSTRALIA
Our focus is your vision

MD Research News

Issue 221

Monday 2 March, 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

Retina. 2015 Feb 24. [Epub ahead of print]

RELATIONSHIP BETWEEN VISUAL PROGNOSIS AND DELAY OF INTRAVITREAL INJECTION OF RANIBIZUMAB WHEN TREATING AGE-RELATED MACULAR DEGENERATION.

Takahashi H, Ohkubo Y, Sato A, et al

BACKGROUND: In age-related macular degeneration, various factors in clinical practice cause delays to arise between the time exudative change is observed and the time anti-vascular endothelial growth factor drugs are actually injected. We investigated the influence of injection delay on prognosis.

METHODS: Subjects were 50 eyes (50 patients from 2 hospitals) that were administered ranibizumab monotherapy for age-related macular degeneration for 1 year since exudative change was first observed. We investigated the mean number of delay days for each injection.

RESULTS: Mean injection delay was between 0 and 104 days. Significant prognostic factors for visual acuity were initial best-corrected visual acuity ($P < 0.01$) and mean injection delay ($P = 0.03$). We estimated that for an initial best-corrected visual acuity of 0.40 logMAR unit (20/50 Snellen equivalent), the respective best-corrected visual acuity values after 1 year for mean injection delays of 0, 7, 14, 28, and 56 days would be 0.22 (20/33), 0.24 (20/35), 0.26 (20/37), 0.31 (20/40), and 0.39 (20/49). For an initial best-corrected visual acuity of 0.097 (20/25), the respective values would be 0.054 (20/23), 0.075 (20/24), 0.10 (20/25), 0.14 (20/28), and 0.22 (20/33).

CONCLUSION: Long-term visual acuity prognosis worsened when scheduling problems delayed intravitreal injection of anti-vascular endothelial growth factor drugs.

PMID: 25719984 [PubMed - as supplied by publisher]

Eye (Lond). 2015 Feb 27. [Epub ahead of print]

Blood flow velocity measured using the Retinal Function Imager predicts successful ranibizumab treatment in neovascular age-related macular degeneration: early prospective cohort study.

Böhni SC, Howell JP, Bittner M, et al.

Purpose: Anti-VEGF treatment has a potent vasoconstrictive effect. Early changes of retinal blood flow velocity (RBFV) measured using the Retinal Function Imager (RFI) combined with indicators of vascular status may help in predicting the visual outcome 1 month post injection in patients with neovascular age-

related macular degeneration (nvAMD) under ranibizumab treatment. To develop a simple prediction model based on the change in RBFV 3 days post injection and indicators of a patient's vascular status to assess the probability of a successful visual outcome 1 month post injection.

Methods: RBFV measured using RFI were prospectively collected pre-injection and 3 days post injection in 18 eyes of 15 patients. Indicators of vascular status (history of hypertension, diabetes mellitus without retinal affection, and smoking) were assessed by medical history. By univariate analyses, parameters associated with visual outcome were weighted (-1 to 6 points). A multivariate logistic regression model with the categorized visual outcome parameter (≥0 letters gained after 1 month) as the dependent variate and the sum score as the independent variate (continuous scale) was used to estimate the score value-specific probabilities of letters gained ≥0 1 month post injection.

Results: The indicators of vascular status negatively influenced the likelihood of a letter gain ≥0 whereas an increase in the arterial RBFV strongly increased it. The area under the receiver operating characteristics curve for these parameters investigated was 0.71 (95% CI: 0.43-1.00).

Conclusion: Changes in the arterial RBFV following 3 days after ranibizumab injection combined with three indicators of the vascular status identified nvAMD patients with favorable visual outcome accurately.

PMID: 25721520 [PubMed - as supplied by publisher]

Sci Rep. 2015 Feb 27;5:8627.

Intravitreal Combination of Dexamethasone Sodium Phosphate and Bevacizumab in The Treatment of Exudative AMD.

Vakalis N, Echiadis G, Pervena A, et al

Abstract: The purpose of this study is to investigate the efficacy and safety of intravitreal dexamethasone sodium phosphate (DSP) combined with bevacizumab for the treatment of neovascular age-related macular degeneration (AMD). In this non comparative case study, 30 eyes of 27 patients with CNV due to AMD received intravitreal DSP (0.2 mg) and bevacizumab (1.25 mg) during a 6-month PRN (pro re nata) dosing regimen. Visual acuity, macular thickness and intraocular pressure (IOP) were monitored and recorded. After 6 months, mean retinal thickness decreased from 423.5 ± 75.3 to 228.2 ± 34.5 and mean visual acuity improved from 0.9 ± 0.39 logMAR to 0.53 ± 0.34 (p = 0.001) logMAR. During the trial period, 81 intravitreal injections were performed in 30 eyes, thus the mean number of injections per eye was 2.7 ± 1.1. 86.7% of the eyes required 3 or less injections while only 13.3% needed 4 or more injections. None of the patients, phakic or pseudophakic, manifested an elevation of IOP during the treatment, ranging between 12 and 22 mmHg. Combined DSP and bevacizumab offers encouraging results in the challenge of AMD treatment, providing immediate response of macular edema, reduced number of intravitreal injections and stabilization or improvement of visual acuity.

PMID: 25720826 [PubMed - in process]

JAMA Ophthalmol. 2015 Feb 26. [Epub ahead of print]

Repeated Intravitreous Ranibizumab Injections for Diabetic Macular Edema and the Risk of Sustained Elevation of Intraocular Pressure or the Need for Ocular Hypotensive Treatment.

Bressler SB, Almukhtar T, Bhorade A, et al

Importance: For the management of retinal disease, the use of intravitreous injections of anti-vascular endothelial growth factor has increased. Recent reports have suggested that this therapy may cause sustained elevation of intraocular pressure (IOP) and may potentially increase the risk of glaucoma for patients with retinal disease.

Objective: To assess the risk of sustained IOP elevation or the need for IOP-lowering treatments for eyes with diabetic macular edema following repeated intravitreous injections of ranibizumab.

Design, Setting, and Participants: An exploratory analysis was conducted within a Diabetic Retinopathy Clinical Research Network randomized clinical trial. Study enrollment dates were from March 20, 2007, to December 17, 2008. Of 582 eyes (of 486 participants) with center-involved diabetic macular edema and no preexisting open-angle glaucoma, 260 were randomly assigned to receive a sham injection plus focal/grid laser treatment, and 322 were randomly assigned to receive ranibizumab plus deferred or prompt focal/grid laser treatment.

Main Outcomes and Measures: The cumulative probability of sustained IOP elevation, defined as IOP of at least 22 mm Hg and an increase of at least 6 mm Hg from baseline at 2 consecutive visits, or the initiation or augmentation of ocular hypotensive therapy, through 3 years of follow-up.

Results: The mean (SD) baseline IOP in both treatment groups was 16 (3) mm Hg (range, 5-24 mm Hg). The cumulative probability of sustained IOP elevation or of initiation or augmentation of ocular hypotensive therapy by 3 years, after repeated ranibizumab injections, was 9.5% for the participants who received ranibizumab plus prompt or deferred focal/grid laser treatment vs 3.4% for the participants who received a sham injection plus focal/grid laser treatment (difference, 6.1% [99% CI, -0.2% to 12.3%]; hazard ratio, 2.9 [99% CI 1.0-7.9]; P = .01). The distribution of IOP and the change in IOP from baseline at each visit through 3 years were similar in each group.

Conclusions and Relevance: In eyes with center-involved diabetic macular edema and no prior open-angle glaucoma, repeated intravitreous injections of ranibizumab may increase the risk of sustained IOP elevation or the need for ocular hypotensive treatment. Clinicians should be aware of this risk and should consider this information when following up with patients who have received intravitreous injections of anti-vascular endothelial growth factor for the treatment of diabetic macular edema.

PMID: 25719991 [PubMed - as supplied by publisher]

Int J Ophthalmol. 2015 Feb 18;8(1):138-47.

Bevacizumab versus ranibizumab for neovascular age-related macular degeneration: a Meta-analysis.

Wang WJ, Chen J, Zhang XL, et al

AIM: To systematically compare the efficacy and safety of off-label bevacizumab versus licensed ranibizumab intravitreal injections as well as monthly regimen versus pro re nata [PRN (as needed)] regimen in the treatment of neovascular age-related macular degeneration (nAMD).

METHODS: Relevant publications were identified through automatically retrieve of database and manually retrieving. The methodological quality of studies included was assessed using the Jadad score and the risk-of-bias assessment. The efficacy estimates were measured by the weight mean difference (WMD) for the improvement of best-corrected visual acuity (BCVA) and central retinal thickness (CRT) reduction. The safety estimates were measured by odds ratios (OR) for adverse events rates. Statistical analysis was conducted by Revman 5.2.7.

RESULTS: Seven studies were included in the Meta-analysis. There were no statistically significant differences between bevacizumab and ranibizumab in BCVA at 1 and 2y (P=0.37, P=0.18, respectively), However, both drugs has better BCVA given monthly than given as needed at 1 and 2y (P<0.05). The results demonstrated the mean decrease in CRT was less in bevacizumab group than ranibizumab group at 1y (P<0.05), while the difference was not significant at 2y (P=0.24). Treatment monthly gained much more decrease in CRT at 1 and 2y (P<0.005). There were no differences between drugs in the rates of death, arterial thrombotic events and venous thrombotic events (P=0.41, P=0.55, P=0.10, respectively), while the rates of medical dictionary for regulatory activities (MedDAR) system organ class events and ≥1 systemic serious adverse events were higher in bevacizumab group than ranibizumab group (P<0.05). But

the incidences of death, arterial thrombotic events, venous thrombotic events, MedDAR system organ class events as well as ≥1 systemic serious adverse events were not statistically different between both treatment regimens of monthly and as needed (P=0.14, P=0.76, P=0.73, P=0.12, P=0.11, respectively).

CONCLUSION: Bevacizumab was equivalent to ranibizumab for BCVA, however bevacizumab tended to gain less decrease in CRT and had higher rates of serious adverse events. Compared with treatment as needed, treatment monthly showed superior efficacy in BCVA improvement and CRT reduction, while the rates of adverse events were similar in the two dosing regimens.

PMID: 25709924 [PubMed] PMCID: PMC4325258

J Ophthalmic Vis Res. 2014 Oct-Dec;9(4):469-77.

Photodynamic Therapy and Intravitreal Bevacizumab with Versus without Triamcinolone for Neovascular Age-related Macular Degeneration; a Randomized Clinical Trial.

Piri N, Ahmadieh H, Taei R, et al.

PURPOSE: To compare the outcomes of photodynamic therapy (PDT) combined with intravitreal bevacizumab (IVB) with versus without intravitreal triamcinolone (IVT) in neovascular age-related macular degeneration (AMD).

METHODS: Eighty-four eyes with active CNV secondary to AMD with no prior treatment were enrolled and followed for 1-year. Eligible eyes were randomly assigned to either PDT/IVB or PDT/IVB/IVT. The main outcome measure was change in best-corrected visual acuity (BCVA).

RESULTS: Mean patient age was 71 ± 9 years. BCVA changes from baseline were statistically significant in both study arms at all follow-up intervals, however no significant difference was observed between the two groups regarding BCVA changes at week 12 (95% CI:-0.11-0.12 LogMAR) and other time points (all P > 0.6). Mixed model analysis revealed a significant effect from age (P < 0.001), pigment epithelial detachment (P = 0.009) and baseline BCVA (P < 0.001) on visual improvement. Significant central macular thickness (CMT) reduction occurred at all-time points as compared to baseline in both groups which was comparable between the study arms. There was no significant difference between the study arms in terms of retreatment rate (P = 0.1) and survival to the first repeat IVB injection (P = 0.065).

CONCLUSION: Additional low-dose IVT to a PDT/IVB regimen for neovascular AMD provided no beneficial effects in terms BCVA or CMT, yet demonstrated a trend toward extending the injection-free period.

PMID: 25709773 [PubMed] PMCID: PMC4329708

J Ophthalmic Vis Res. 2014 Oct-Dec;9(4):449-52.

Changes in Retinal Nerve Fiber Layer Thickness after Two Intravitreal Bevacizumab Injections for Wet Type Age-related Macular Degeneration.

Entezari M, Ramezani A, Yaseri M.

PURPOSE: To evaluate the effect of two intravitreal bevacizumab (IVB) injections on peripapillary retinal nerve fiber layer (RNFL) thickness in patients with wet type age-related macular degeneration (ARMD).

METHODS: This prospective interventional case series included 18 eyes of 18 patients receiving two IVB injections within a 6 weeks interval for treatment of wet type ARMD. Peripapillary RNFL thickness was measured prior to the first injection, and 12 and 24 weeks afterwards by optical coherence tomography (3D OCT-1000, Topcon Corporation, Tokyo, Japan). Mean RNFL thickness and values in the four peripapillary quadrants were compared at baseline, and 12 and 24 weeks after initial injection.

RESULTS: Mean RNFL thickness was 89 ± 21 μm at baseline which was significantly reduced to 82 ± 15

μm at 12 weeks (P = 0.021). At final follow-up (week 24), mean RNFL thickness reached 87 ± 23 μm and was comparable to baseline values (P = 0.356). Only the temporal quadrant showed a significant reduction in RNFL thickness at 12 weeks (P = 0.033); this quadrant followed the same pattern of change as the mean RNFL thickness, becoming comparable to pre-injection values at 24 weeks (P = 0. 298).

CONCLUSION: RNFL thickness may decrease temporarily following two IVB injections in patients with wet type ARMD; however, in the long-term no significant change was detectable from baseline values.

PMID: 25709770 [PubMed] PMCID: PMC4329705

Curr Pharm Des. 2015 Feb 25. [Epub ahead of print]

Anti-VEGF Drugs in Eye Diseases: Local Therapy with Potential Systemic Effects.

Giet MV, Henkel C, Schuchardt M, Tölle M.

Abstract: Vascular endothelial growth factor (VEGF) is one of the main endogenous pro-angiogenic cytokines. Inhibition of the VEGF signaling pathways is an effective treatment for cancer patients. In addition, local anti-VEGF therapy was developed and established to treat proliferative diabetic retinopathy, age-related macular degeneration and retinal vein occlusion. For systemic administration of anti-VEGF drugs, serious side effects including hypertension or renal disorders have been observed. Evidence suggests that systemic effects might occur or develop in long-term treatment, despite limited resorption and minimal local side effects. Here, only limited data from clinical studies are available. The VEGF system is delicately balanced, and changes might result in deleterious effects. This review provides a brief overview of the VEGF-system, and summarizes its relevance in proliferative eye diseases. The anti-VEGF drugs used to treat different disease conditions are discussed with their local and systemic side effects associated with local anti-VEGF therapies are addressed.

PMID: 25714990 [PubMed - as supplied by publisher]

Arq Bras Oftalmol. 2015 Jan-Feb;78(1):32-5.

Survey: technique of performing intravitreal injection among members of the Brazilian Retina and Vitreous Society (SBRV).

Shiroma HF, Farah ME, Takahashi WY, et al.

PURPOSE: To evaluate and describe the precautions involved in the technique of intravitreal injection of antiangiogenic drugs adopted by the ophthalmologists who are members of the Brazilian Society of Retina and Vitreous (SBRV).

METHODS: A questionnaire containing 22 questions related to precautions taken before, during, and after intravitreal injection was sent electronically to 920 members of SBRV between November 15, 2013 and April 31, 2014.

RESULTS: 352 responses (38%) were obtained. There was a predominance of men (76%) from the southwest region of Brazil (51%). The professional experience varied between 6 and 15 years after medical specialization (50%). Most professionals (76%) performed an average of 1 to 10 intravitreal injections a week, and 88% of the procedures were performed in the operating room using povidone iodine (99%), sterile gloves, and blepharostat (94%). For inducing topical anesthesia, usage of anesthetic eye drops was the most used technique (65%). Ranibizumab (Lucentis®) was the most common drug (55%), and age-related macular degeneration (AMD) was the most treated disease (57%). Regarding the complications treated, 6% of the ophthalmologists had treated at least one case of retinal detachment, 20% had treated cases of endophthalmitis, 9% had treated cases of vitreous hemorrhage, and 12% had encountered cases of crystalline lens touch.

CONCLUSION: Intravitreal injection is a procedure routinely performed by retina specialists and has a low incidence of complications. Performing the procedure in the operating room using an aseptic technique was preferred by most of the respondents. Ranibizumab was the most used drug, and AMD was the most treated disease.

PMID: 25714535 [PubMed - in process]

Ophthalmic Surg Lasers Imaging Retina. 2015 Feb 1;46(2):275-8.

Regression of drusen after combined treatment using photodynamic therapy with verteporfin and ranibizumab.

Novais EA, Badaró E, Regatieri CV, et al

Abstract: Drusen are the clinical hallmark of age-related macular degeneration. The regression of these deposits in patients treated with argon, krypton, or diode laser photocoagulation has been reported previously. However, previous protocols with conventional laser for drusen may result in retinal pigment epithelium (RPE) damage and unwanted scotomas. The authors report a case of complete regression of soft drusen in a 65-year-old man with central visual loss and metamorphopsia due to a drusenoid RPE detachment and soft drusen who underwent reduced-fluence photodynamic therapy (PDT) and three monthly intravitreal injections of ranibizumab. Reduced-fluence PDT combined with anti-VEGF therapy may reduce drusen without inducing RPE cell damage.

PMID: 25707058 [PubMed - in process]

Ophthalmic Surg Lasers Imaging Retina. 2015 Feb 1;46(2):195-200. doi: 10.3928/23258160-20150213-18.

Quantitative OCT Subanalysis of Eyes With Choroidal Neovascularization Switched From Multiple Injections of Bevacizumab or Ranibizumab to Intravitreal Aflibercept.

Hariri A, Diniz B, Fou LV, et al.

BACKGROUND AND OBJECTIVE: To assess the early therapeutic response after switching from multiple injections of bevacizumab or ranibizumab to aflibercept in eyes with neovascular age-related macular degeneration (AMD).

PATIENTS AND METHODS: SD-OCT scans of patients with neovascular AMD that was suboptimally responsive to multiple injections of bevacizumab or ranibizumab who were switched to aflibercept were analyzed. After segmenting these scans, the relevant volumes were computed and compared at the various time points by Student's t test.

RESULTS: After switching to aflibercept, converse to the outcome of the last injection of bevacizumab or ranibizumab, statistically significant decreases of 0.32 mm(3) in neurosensory retinal volume, 0.08 mm(3) in subretinal fluid, and 0.56 mm(3) in pigment epithelial detachment were observed (P = .01, .04, and .001, respectively). The mean ETDRS visual acuity increased from 62 to 65 letters after switching (P = .04). These favorable outcomes were sustained after three monthly injections of the new drug.

CONCLUSION: Switching to aflibercept therapy in eyes with persistent fluid after multiple intravitreal injections of bevacizumab or ranibizumab was associated with an early reduction in all fluid compartments and improvement in visual acuity. [Ophthalmic Surg Lasers Imaging Retina. 2015;46:195-200.].

PMID: 25707044 [PubMed - in process]

Drug Saf. 2015 Feb 22. [Epub ahead of print]

Comparative Safety and Tolerability of Anti-VEGF Therapy in Age-Related Macular Degeneration.

Modi YS, Tanchon C, Ehlers JP.

Abstract: Neovascular age-related macular degeneration (NVAMD) is one of the leading causes of blindness. Over the last decade, the treatment of NVAMD has been revolutionized by the development of intravitreal anti-vascular endothelial growth factor (VEGF) therapies. Several anti-VEGF medications are used for the treatment of NVAMD. The safety and tolerability of these medications deserve review given the high prevalence of NVAMD and the significant utilization of these medications. Numerous large randomized clinical trials have not shown any definitive differential safety relative to ocular or systemic safety of these medications. Intravitreal anti-VEGF therapy does appear to impact systemic VEGF levels, but the implications of these changes remain unclear. One unique safety concern relates drug compounding and the potential risks of contamination, specifically for bevacizumab. Continued surveillance for systemic safety concerns, particularly for rare events, is merited. Overall, these medications are well tolerated and effective in the treatment of NVAMD.

PMID: 25700714 [PubMed - as supplied by publisher]

Ophthalmology. 2015 Mar;122(3):e18-9.

Re: Bakri et al.: Intraocular pressure in eyes receiving monthly ranibizumab in 2 pivotal age-related macular degeneration clinical trials (Ophthalmology 2014;121:1102-8).

Zygoura V, Kopsachilis N, Carifi G.

PMID: 25703469 [PubMed - in process]

Other treatment & diagnosis

Clin Ophthalmol. 2015 Feb 11;9:297-304.

Widespread choroidal thickening and abnormal midperipheral fundus autofluorescence characterize exudative age-related macular degeneration with choroidal vascular hyperpermeability.

Nomura Y, Takahashi H, Tan X, et al.

PURPOSE: To investigate the clinical findings that characterize exudative age-related macular degeneration (AMD) with choroidal vascular hyperpermeability (CVH).

DESIGN: Retrospective comparative study.

PARTICIPANTS: Forty-eight consecutive patients attending the outpatient clinic of Tokyo University Hospital between May 2013 and July 2013.

METHODS: The presence or absence of CVH was determined with indocyanine green angiography performed at the latest visit. When CVH was observed, the eye was categorized as CVH(+) AMD, otherwise it was categorized as CVH(-) AMD. Using high-penetration optical coherence tomography, we measured choroidal thickness at the fovea and at four midperipheral areas (mean choroidal thickness at points on 6- and 9-papilla diameter circles superior, inferior, temporal, and nasal to the fovea). Ultrawide field retinal imaging was used to investigate abnormalities in midperipheral fundus autofluorescence (FAF). Choroidal thickness and the proportion of FAF abnormalities were compared between the CVH(+) AMD and CVH(-) AMD eyes and between eyes with polypoidal choroidal vasculopathy and typical AMD. Multiple regression analysis was used to control for treatment history and other characteristics.

RESULTS: CVH was observed in 17 cases. Choroidal thickness was higher in the CVH(+) AMD eyes than in the CVH(-) AMD eyes at the fovea (325 µm versus 229 µm, respectively; P=0.0010, t-test), superior point (277 µm versus 215 µm, respectively; P=0.0021, t-test), inferior point (225 µm versus 161 µm, respectively; P=0.0002, t-test), and nasal point (202 µm versus 165 µm, respectively; P=0.042, t-test). The significance was maintained after controlling for possible confounders. The choroid was thicker at the fovea and at the inferior point in polypoidal choroidal vasculopathy than in typical AMD. The rate of midperipheral FAF abnormality was significantly higher in the CVH(+) AMD eyes than in the CVH(-) AMD eyes (82% versus 48%, respectively; P=0.031).

CONCLUSION: AMD with CVH is associated with widespread choroidal thickening and peripheral FAF abnormalities.

PMID: 25709392 [PubMed] PMCID: PMC4334323

Ophthalmic Surg Lasers Imaging Retina. 2015 Feb 1;46(2):229-34.

Neovascular age-related macular degeneration associated with no light perception.

Brown GC, Basha MM, Brown MM.

BACKGROUND AND OBJECTIVE: To study eyes with no light perception (NLP) occurring secondary to neovascular age-related macular degeneration (AMD).

PATIENTS AND METHODS: Records of consecutive patients with neovascular AMD seen during a 10-year period were reviewed to ascertain which patients had NLP due to neovascular AMD.

RESULTS: Ten of 1,150 patients (0.9%) with neovascular AMD had NLP in one eye (study eye) from neovascular AMD. All 10 patients had bilateral neovascular AMD. Each study eye had a large macular disciform scar and 360° peripapillary subretinal fibrovascular tissue. Seven of nine (78%) study eyes had optic disc pallor, versus none of eight fellow eyes (P = .04). Mean fellow eye vision was 20/231, ranging from 20/50 to NLP (P = .006 vs study eyes). No seeing fellow eye had choroidal neovascularization encircling the optic disc (P = .0004).

CONCLUSION: NLP from neovascular AMD is associated with 360° peripapillary subretinal fibrosis. This fibrosis may cause chronic ischemic optic neuropathy contributing to extinguished vision.

PMID: 25707049 [PubMed - in process]

Br J Ophthalmol. 2015 Feb 26.[Epub ahead of print]

En face swept-source optical coherence tomography in neovascular age-related macular degeneration.

Flores-Moreno I, Arias-Barquet L, Rubio-Caso MJ, et al.

PURPOSE: To describe en face swept-source optical coherence tomography (SS-OCT) findings in the retinal pigment epithelium (RPE) and choroid and to correlate them with fluorescein angiography (FA) and/or indocyanine green angiography (ICGA) in neovascular age-related macular degeneration (AMD).

METHODS: Thirty-eight eyes with the recent diagnosis of neovascular AMD were imaged using an SS-OCT system. En face images were obtained at RPE, choriocapillaris, Sattler's layer and Haller's layer level. Analysis of the images and correlation with colour fundus photographs, FA, ICGA in selected cases, were made.

RESULTS: En face images at RPE level revealed changes in all eyes. The neovascular complex appeared hyper-reflective in 9 of 38 eyes (23.7%), and in 29 of 38 eyes (76.3%), it was hyporeflective. The

choriocapillaris en face image showed pathological changes in all eyes as well, and in 20 out of 38 eyes (52.6%), the alterations were hyper-reflective, while 18 of 38 eyes (47.4%) showed hyporeflective changes. Twenty (52.6%) eyes and 19 (50.0%) had a hyper-reflective lesion in Sattler's layer and Haller's layer, respectively, and 15 (39.4%) cases showed a hyporeflective lesion in both layers. No differences were found between the neovascular complex area, horizontal and vertical diameters, measured in the en face image and FA (p=0.171, p=0.061, p=0.133, respectively). Hyporeflective changes were predominant at RPE level and hyper-reflective at choriocapillaris, Sattler's and Haller's layers.

CONCLUSIONS: En face SS-OCT is a rapid, non-invasive, high-resolution, promising technology, which allows a complementary study to angiography of neovascular AMD. There is a correlation between angiography and en face SS-OCT images in neovascular AMD.

PMID: 25722493 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2015 Feb 26. [Epub ahead of print]

Choroidal Vascular Hyperpermeability and Punctate Hyperfluorescent Spot in Choroidal Neovascularization.

Kim JH, Chang YS, Lee TG, Kim CG.

Purpose: To evaluate the prevalence of choroidal vascular hyperpermeability and punctate hyperfluorescent spots in eyes with choroidal neovascularization (CNV).

Methods: This retrospective, observational study included 382 eyes with typical exudative age-related macular degeneration (AMD, 97 eyes), polypoidal choroidal vasculopathy (PCV, 163 eyes), retinal angiomatous proliferation (RAP, 37 eyes), or myopic CNV (86 eyes). The prevalence of choroidal vascular hyperpermeability and punctate hyperfluorescent spots was estimated based on available indocyanine green angiography (ICGA) images.

Results: Choroidal vascular hyperpermeability was noted in 12.4% (12 eyes) and 26.9% (42 eyes) of eyes with typical exudative AMD and PCV, respectively. Choroidal vascular hyperpermeability was not noted in any eye with RAP or myopic CNV. Punctate hyperfluorescent spots were noted in 43.3% (42 eyes), 72.4% (118 eyes), 10.8% (4 eyes), and 4.7% (4 eyes) of eyes with typical exudative AMD, PCV, RAP, and myopic CNV, respectively. Of the 56 eyes with choroidal vascular hyperpermeability, punctate hyperfluorescent spots were noted in 55 eyes (98.2%).

Conclusions: Choroidal vascular hyperpermeability and punctate hyperfluorescent spots may have a common pathophysiology. Although choroidal vascular hyperpermeability and punctate hyperfluorescent spots have been thought to be associated with pathologic conditions, the markedly low prevalence of these findings in eyes with RAP and myopic CNV may not be a normal finding. It is possible that compromised choroidal perfusion, with or without associated with choroidal thinning, may lead the low prevalence of these abnormalities in eyes with these two disorders.

PMID: 25722216 [PubMed - as supplied by publisher]

Allergy Asthma Proc. 2015 Mar;36(2):123-9.

Central serous chorioretinopathy secondary to corticosteroids in patients with atopic disease.

Ricketti PA, Unkle DW, Cleri DJ, et al.

Abstract: Central serous chorioretinopathy (CSCR) is of unknown etiology and is the most common cause of retinopathy after age-related macular degeneration, diabetic retinopathy, and retinal vein occlusion. Vision loss results from fluid leakage and serous detachment in the macula. Five percent of patients develop chronic CSCR. It is predominantly found in middle-aged men (age-adjusted rates per 100,000: 9.9

for men and 1.7 for women) and is usually unilateral and reversible. Three-quarters of CSCR patients resolve within 3 months but 45% have recurrences, usually with only minor visual acuity changes. Risk factors include type A personality, emotional stress, elevated catecholamines, hypertension, pregnancy, organ transplantation, increased levels of endogenous cortisol, psychopharmacologic medication, use of phosphodiesterase 5 inhibitors, obstructive sleep apnea, Helicobacter pylori infection, or treatment with corticosteroids. Five percent of patients develop chronic disease as a result of subretinal fibrin formation within the blister. CSCR is often bilateral, multifocal, and recurrent, and may be associated with subretinal fibrin formation within the blister. Permanent loss of vision may result from subretinal fibrin-fibrosis with scarring of the macula. Corticosteroid-associated CSCR occurs bilaterally in 20% of patients. Steroid-associated therapy may begin days to years after therapy with any form of drug delivery. We present three atopic patients who presented at various times after oral, inhaled, intranasal, and topical corticosteroid therapy. One patient developed CSCR after three separate types of administration of corticosteroids, which, to our knowledge, has not been observed in the literature.

PMID: 25715240 [PubMed - in process]

Curr Opin Neurobiol. 2015 Feb 20;34C:74-78. [Epub ahead of print]

Optopharmacological tools for restoring visual function in degenerative retinal diseases.

Tochitsky I, Kramer RH.

Abstract: Retinitis pigmentosa (RP) and age-related macular degeneration (AMD) are progressive retinal diseases that result from the death of rod and cone photoreceptors, ultimately leading to blindness. The only currently approved vision restoration treatment employs an implanted retinal 'chip' as a prosthetic device to electrically stimulate retinal neurons that survive after the photoreceptors are gone, thereby restoring light-driven neural signaling to the brain. Alternative strategies have been proposed, which would utilize optogenetic or optopharmacological tools to enable direct optical stimulation of surviving retinal neurons. Here, we review the latest studies evaluating the feasibility of these molecular tools as potential therapeutics for restoring visual function in human blinding disease.

PMID: 25706312 [PubMed - as supplied by publisher]

Pathogenesis

Monoclon Antib Immunodiagn Immunother. 2015 Feb;34(1):1-6.

Anti-Mouse Properdin TSR 5/6 Monoclonal Antibodies Block Complement Alternative Pathway-dependent Pathogenesis.

Bertram P, Akk AM, Zhou HF, et al

Abstract: The complement alternative pathway (AP) is a major contributor to a broad and growing spectrum of diseases that includes age-related macular degeneration, atypical hemolytic uremic syndrome, and preeclampsia. As a result, there is much interest in the therapeutic disruption of AP activity. Properdin, the only positive regulator of the AP, is a particularly promising AP target. Several issues need to be clarified before the potential for properdin-directed therapy can be realized. In this report we use a portion of the mouse properdin protein, expressed in a bacterial system, to raise rabbit polyclonal and hamster monoclonal antibodies that block properdin-dependent pathogenesis. These antibodies, when employed with AP-dependent mouse disease models, can help evaluate the feasibility of properdin-directed therapy.

PMID: 25723276 [PubMed - in process]

Ultrasound Med Biol. 2015 Feb 23. [Epub ahead of print]

Effects of Low-Intensity Ultrasound on Oxidative Damage in Retinal Pigment Epithelial Cells in Vitro.

Kim NK, Kim CY, Choi MJ, Park SR, Choi BH.

Abstract: Oxidative stress in retinal pigment epithelium (RPE) is one of the key causative factors of RPE injury in age-related macular degeneration (AMD). Low-intensity ultrasound (LIUS) less than 1 W/cm2 in intensity has been found to have cytoprotective and anti-inflammatory effects in many cell types and diseases. In this study, we investigated for the first time the feasibility of using LIUS to protect RPE cells from oxidative damage. ARPE-19 cells were treated with H2O2 (an exogenous source of reactive oxygen species) or L-buthionine-(S,R)-sulfoximine (BSO), a glutathione synthase inhibitor, and exposed immediately to LIUS at intensities of 50, 100 and 200 mW/cm2 and a frequency of 1 MHz for 20 min. Both H2O2 and BSO increased the percentage of cells positive for mitochondrial reactive oxygen species at 1 h, but not at 24 h. Co-treatment with LIUS clearly repressed these cells similarly at all intensities by approximately 34%-43% for H2O2 and 24%-25% for BSO ($p < 0.05$). The percentage of cells with mitochondrial membrane depolarization also increased with H2O2 and BSO treatment, particularly at 1 h, and decreased by approximately 60% with LIUS at 100 mW/cm2 ($p < 0.05$). The amount of intracellular calcium ion ([Ca2+]i) was elevated only by BSO at 24 h and was also significantly diminished, by approximately 45%, by LIUS at 100 mW/cm2 ($p < 0.05$). Both H2O2 and BSO significantly hampered cell viability at 24 h, but LIUS at 100 mW/cm2 restored only BSO-induced cell viability by approximately 2.7-fold ($p < 0.05$). This study illustrated that LIUS has a protective effect on RPE cells against oxidative damage caused by BSO, an endogenous mitochondrial reactive oxygen species generator. We speculate that LIUS has the potential to treat oxidative damage and related pathologic changes in RPE.

PMID: 25722027 [PubMed - as supplied by publisher]

Anal Chem. 2015 Feb 26. [Epub ahead of print]

Microfluidic Multiculture Assay to Analyze Biomolecular Signaling in Angiogenesis.

Theberge AB, Yu J, Young EW, et al

Abstract: Angiogenesis (the formation of blood vessels from existing blood vessels) plays a critical role in many diseases such as cancer, benign tumors, and macular degeneration. There is a need for cell culture methods capable of dissecting the intricate regulation of angiogenesis within the microenvironment of the vasculature. We have developed a microscale cell-based assay that responds to complex pro- and antiangiogenic soluble factors with an in vitro readout for vessel formation. The power of this system over traditional techniques is that we can incorporate the whole milieu of soluble factors produced by cells in situ into one biological readout (vessel formation), even if the identity of the factors is unknown. We have currently incorporated macrophages, endothelial cells, and fibroblasts into the assay, with the potential to include additional cell types in the future. Importantly, the microfluidic platform is simple to operate and multiplex to test drugs targeting angiogenesis in a more physiologically relevant context. As a proof of concept, we tested the effect of an enzyme inhibitor (targeting matrix metalloproteinase 12) on vessel formation; the triculture microfluidic assay enabled us to capture a dose-dependent effect entirely missed in a simplified coculture assay ($p < 0.0001$). This result underscores the importance of cell-based assays that capture chemical cross-talk occurring between cell types. The microscale dimensions significantly reduce cell consumption compared to conventional well plate platforms, enabling the use of limited primary cells from patients in future investigations and offering the potential to screen therapeutic approaches for individual patients in vitro.

PMID: 25719435 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2015 Feb 24. pii: IOVS-14-15933. doi: 10.1167/iovs.14-15933. [Epub ahead of print]

Serum Leptin and Age-related Macular Degeneration.

Seshasai S, Liao J, Toh QC, et al

Purpose: Leptin, a 167-aminoacid protein secreted by adipocytes has been shown to reduce beta-amyloid deposition and intracellular lipid concentration in animal models, two key pathogenic mechanisms underlying aging. We examined the association between serum leptin levels and age-related macular degeneration (AMD).

Methods: We conducted a population-based case-control study including Chinese and Indian adults aged 40-80 years who participated in the Singapore Epidemiology of Eye Diseases Study (2007-2011). AMD was assessed from retinal photographs graded using a modified Wisconsin Age-Related Maculopathy Grading System (n=423, early = 387, late=36). Controls (n=927) without AMD were frequency matched for age, gender and ethnicity. Serum leptin levels were measured using direct sandwich ELISA.

Results: Participants with AMD had lower levels of leptin compared to those without (mean (SD) = 10.0 (11.5) vs. 12.9 (16.4) ng/mL; p=0.001). Mean levels of leptin among those with late, early and without AMD were 8.8, 10.1 and 12.9 (p-trend= 0.005). In multivariable models adjusting for potential confounders including smoking, body mass index, blood pressure and HDL cholesterol, increasing quartiles of leptin were associated with lower odds of AMD, odds ratio (95% confidence interval) of AMD was 0.56 (0.34-0.92) comparing highest to lowest quartile of serum leptin. In subgroup analyses, the inverse association between leptin and AMD was significant in women, Indian ethnicity and ex-smokers (all P-interaction>0.05).

Conclusions: Higher serum leptin levels were inversely associated with AMD. These findings, if confirmed in prospective studies, may provide insights into new pathogenic pathways and possibly therapeutic targets in AMD.

PMID: 25711634 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2015 Feb;232(2):127-32.

[Physiological basis of the microcirculation: vascular adaptation].[Article in German]

Pries AR.

Abstract: The microcirculation is the functional "business end" of the cardiovascular system. In vessels with diameters below about 300 µm processes including the regulation of perfusion, exchange processes and relevant components of the immune system are localised. A large number of individual mechanisms are involved, including micro-rheology, the endothelial surface layer, vascular permeability, endothelial function, regulation of smooth muscle tone, leukocyte endothelial interaction, vascular adaptation and angiogenesis. The present article focusses mainly on the role of vascular adaptation. Much more than in large vessels, the microcirculation is characterised by constant adaptation to haemodynamic and metabolic signals. In reaction to changes in parenchymal demand, changes of the diameter of existing vessels (by changes in tone or by structural remodelling) as well as generation of new vessels (angiogenesis) or the pruning of vessels are elicited. These mechanisms are part of the so-called "angioadaptation" which is of great clinical relevance for the pathophysiological consequences of hypertension and age-related macular degeneration.

PMID: 25700251 [PubMed - in process]

Front Chem. 2015 Feb 2;3:4.

Nrf2 activation as target to implement therapeutic treatments.

Bocci V, Valacchi G.

Abstract: A chronic increase of oxidative stress is typical of serious pathologies such as myocardial infarction, stroke, chronic limb ischemia, chronic obstructive pulmonary disease (COPD), type II-diabetes, age-related macular degeneration leads to an epic increase of morbidity and mortality in all countries of the world. The initial inflammation followed by an excessive release of reactive oxygen species (ROS) implies a diffused cellular injury that needs to be corrected by an inducible expression of the innate detoxifying and antioxidant system. The transcription factor Nrf2, when properly activated, is able to restore a redox homeostasis and possibly improve human health.

PMID: 25699252 [PubMed] PMCID: PMC4313773

Mediators Inflamm. 2015;2015:690243. Epub 2015 Jan 27.

NLRP3 Inflammasome: Activation and Regulation in Age-Related Macular Degeneration.

Gao J, Liu RT, Cao S, et al

Abstract: Age-related macular degeneration (AMD) is the leading cause of legal blindness in the elderly in industrialized countries. AMD is a multifactorial disease influenced by both genetic and environmental risk factors. Progression of AMD is characterized by an increase in the number and size of drusen, extracellular deposits, which accumulate between the retinal pigment epithelium (RPE) and Bruch's membrane (BM) in outer retina. The major pathways associated with its pathogenesis include oxidative stress and inflammation in the early stages of AMD. Little is known about the interactions among these mechanisms that drive the transition from early to late stages of AMD, such as geographic atrophy (GA) or choroidal neovascularization (CNV). As part of the innate immune system, inflammasome activation has been identified in RPE cells and proposed to be a causal factor for RPE dysfunction and degeneration. Here, we will first review the classic model of inflammasome activation, then discuss the potentials of AMD-related factors to activate the inflammasome in both nonocular immune cells and RPE cells, and finally introduce several novel mechanisms for regulating the inflammasome activity.

PMID: 25698849 [PubMed - as supplied by publisher] PMCID: PMC4324923

Orv Hetil. 2015 Mar 1;156(9):358-65.

[The age-related macular degeneration as a vascular disease/part of systemic vasculopathy: contributions to its pathogenesis].[Article in Hungarian]

Fischer T.

Abstract: The wall of blood vessels including those in choroids may be harmed by several repeated and/or prolonged mechanical, physical, chemical, microbiological, immunologic, and genetic impacts (risk factors), which may trigger a protracted response, the so-called host defense response. As a consequence, pathological changes resulting in vascular injury (e. g. atherosclerosis, age-related macular degeneration) may be evolved. Risk factors can also act directly on the endothelium through an increased production of reactive oxygen species promoting an endothelial activation, which leads to endothelial dysfunction, the onset of vascular disease. Thus, endothelial dysfunction is a link between the harmful stimulus and vascular injury; any kind of harmful stimuli may trigger the defensive chain that results in inflammation that may lead to vascular injury. It has been shown that even early age-related macular degeneration is associated with the presence of diffuse arterial disease and patients with early age-related macular degeneration demonstrate signs of systemic and retinal vascular alterations. Chronic inflammation, a feature of AMD, is tightly linked to diseases associated with ED: AMD is accompanied by a general inflammatory response, in the form of complement system activation, similar to that observed in degenerative vascular diseases such as atherosclerosis. All these facts indicate that age-related macular degeneration may be a vascular disease (or part of a systemic vasculopathy). This recognition could have therapeutic implications because restoration of endothelial dysfunction may prevent the development or

improve vascular disease resulting in prevention or improvement of age-related macular degeneration as well. Orv. Hetil., 2015, 156(9), 358-365.

PMID: 25702256 [PubMed - in process]

Eur J Pharm Biopharm. 2015 Feb 19. [Epub ahead of print]

Intracellular delivery of dendrimer triamcinolone acetonide conjugates into microglial and human retinal pigment epithelial cells.

Kambhampati SP, Mishra MK, Mastorakos P, et al.

Abstract: Triamcinolone acetonide (TA) is a potent, intermediate-acting, steroid that has anti-inflammatory and anti-angiogenic activity. Intravitreal administration of TA has been used for diabetic macular edema, proliferative diabetic retinopathy and exudative age-related macular degeneration (AMD). However, the hydrophobicity, lack of solubility, and the side effects limit its effectiveness in the treatment of retinal diseases. In this study, we explore a PAMAM dendrimer-TA conjugate (D-TA) as a potential strategy to improve intracellular delivery and efficacy of TA to target cells. The conjugates were prepared with a high drug payload (~21%) and were readily soluble in saline. Compared to free TA, D-TA demonstrated a significantly improved toxicity profile in two important target [microglial and human retinal pigment epithelium (RPE)] cells. The D-TA was ~100-fold more effective than free TA in its anti-inflammatory activity (measured in microglia), and in suppressing VEGF production (in hypoxic RPE cells). Dendrimer-based delivery may improve the efficacy of TA toward both its key targets of inflammation and VEGF production, with significant clinical implications.

PMID: 25701805 [PubMed - as supplied by publisher]

Epidemiology

N Z Med J. 2015 Feb 20;128(1409):44-55.

Prevalence predictions for age-related macular degeneration in New Zealand have implications for provision of healthcare services.

Worsley D, Worsley A.

AIM: To predict the prevalence of age-related macular degeneration (AMD) in New Zealand from 2014 through to 2026.

METHOD: Prevalence estimates for AMD in New Zealand for 2014 through to 2026 were generated by applying ethnic prevalence rate estimates for any, early and late AMD to New Zealand population projections for European, Maori, Pacific and Asian peoples.

RESULTS: The prevalence of any AMD in New Zealand for the 45-85 year age group is estimated to be 184,400 in 2014 (10.3% of this age group) and increase 12.9% to 208,200 (9.9% of this age group) in 2026. For 2014 and 2026 respectively, early disease is estimated to be 167,500 and increase to 189,200 and late disease is estimated to be 7,600 and increase to 8,600.

CONCLUSION: The prevalence of AMD is expected to markedly increase from 2014 through 2026. New Zealand has the lowest funding of treatment for AMD in the OECD and a relatively low ophthalmic workforce. As such, there is a need to plan for an increasing demand for intervention strategies and associated ophthalmic services.

PMID: 25721961 [PubMed - in process]

Br J Ophthalmol. 2015 Feb 23. [Epub ahead of print]

Prevalence of age-related macular degeneration in the Republic of Ireland.

Akuffo KO, Nolan J, Stack J, et al

BACKGROUND: Age-related macular degeneration (AMD) remains the most common cause of visual loss among subjects over 50 years of age in the developed world. The Irish Longitudinal study on Ageing (TILDA) is a population-based study of subjects aged 50 years or older, designed to investigate factors that influence ageing, and has enabled this investigation of the prevalence of AMD in the Republic of Ireland (ROI).

METHODS: Data collected from a nationally representative sample of community-living older adults aged 50 years and over in ROI over the period November 2009 to July 2011. 5035 participants attended the TILDA health centre for assessment. Retinal photographs were obtained in 4859 of these participants. Retinal grading was performed in a masked fashion using a modified version of the International Classification and Grading System for AMD.

RESULTS: Adjusting for lower response rates among older subjects, the estimated overall prevalence of any AMD was 7.2% (95% CI 6.5% to 7.9%) in the population aged 50 years or older. The estimated prevalence of early AMD was 6.6% (95% CI 5.9% to 7.3%), and the estimated prevalence of late AMD was 0.6% (95% CI 0.4% to 0.8%). Statistically significant associations with AMD included increasing age and family history of the condition.

CONCLUSIONS: This is the first study to provide prevalence estimates of AMD in ROI and will inform eye care professionals and policymakers involved in the delivery and planning of care for those afflicted with this condition.

PMID: 25712825 [PubMed - as supplied by publisher]

Cell Rep. 2015 Feb 24;10(7):1173-86.

ROCK-Isoform-Specific Polarization of Macrophages Associated with Age-Related Macular Degeneration.

Zandi S, Nakao S, Chun KH, et al

Abstract: Age is a major risk factor in age-related macular degeneration (AMD), but the underlying cause is unknown. We find increased Rho-associated kinase (ROCK) signaling and M2 characteristics in eyes of aged mice, revealing immune changes in aging. ROCK isoforms determine macrophage polarization into M1 and M2 subtypes. M2-like macrophages accumulated in AMD, but not in normal eyes, suggesting that these macrophages may be linked to macular degeneration. M2 macrophages injected into the mouse eye exacerbated choroidal neovascular lesions, while M1 macrophages ameliorated them, supporting a causal role for macrophage subtypes in AMD. Selective ROCK2 inhibition with a small molecule decreased M2-like macrophages and choroidal neovascularization. ROCK2 inhibition upregulated M1 markers without affecting macrophage recruitment, underlining the plasticity of these macrophages. These results reveal age-induced innate immune imbalance as underlying AMD pathogenesis. Targeting macrophage plasticity opens up new possibilities for more effective AMD treatment.

PMID: 25704819 [PubMed - in process]

Diet, lifestyle and low vision

Arch Biochem Biophys. 2015 Feb 18. [Epub ahead of print]

Role of macular xanthophylls in prevention of common neovascular retinopathies: Retinopathy of

prematurity and diabetic retinopathy.

Gong X, Rubin LP.

Abstract: Retinopathy of prematurity (ROP) and diabetic retinopathy (DR) are important causes of blindness among children and working-age adults, respectively. The development of both diseases involves retinal microvascular degeneration, vessel loss and consequent hypoxic and inflammatory pathologic retinal neovascularization. Mechanistic studies have shown that oxidative stress and subsequent derangement of cell signaling are important factors in disease progression. In eye and vision research, role of the dietary xanthophyll carotenoids, lutein and zeaxanthin, has been more extensively studied in adult onset macular degeneration than these other retinopathies. These carotenoids also may decrease severity of ROP in preterm infants and of DR in working-age adults. A randomized controlled clinical trial of carotenoid supplementation in preterm infants indicated that lutein has functional effects in the neonatal eye and is anti -inflammatory. Three multicenter clinical trials all showed a trend of decreased ROP severity in the lutein supplemented group. Prospective studies on patients with non-proliferative DR indicate serum levels of lutein and zeaxanthin are significantly lower in these patients compared to normal subjects. The present review describes recent advances in lutein and zeaxanthin modulation of oxidative stress and inflammation related to ROP and DR and discusses potential roles of lutein/zeaxanthin in preventing or lessening the risks of disease initiation or progression.

PMID: 25701588 [PubMed - as supplied by publisher]

Int J Ophthalmol. 2015 Feb 18;8(1):11-6.

Lycium barbarum polysaccharides protected human retinal pigment epithelial cells against oxidative stress-induced apoptosis.

Liu L, Lao W, Ji QS, et al

AIM: To investigate the protective effect and its mechanism of lycium barbarum polysaccharides (LBP) against oxidative stress-induced apoptosis in human retinal pigment epithelial cells.

METHODS: ARPE-19 cells, a human retinal pigment epithelial cell lines, were exposed to different concentrations of H2O2 for 24h, then cell viability was measured by Cell Counting Kit-8 (CCK-8) assay to get the properly concentration of H2O2 which can induce half apoptosis of APRE-19. With different concentrations of LBP pretreatment, the ARPE-19 cells were then exposed to appropriate concentration of H2O2, cell apoptosis was detected by flow cytometric analysis. Expression levels of Bcl-2 and Bax were measured by real time quantitative polymerase chain reaction (RT-PCR) technique.

RSULTS: LBP significantly reduced the H2O2-induced ARPE-19 cells' apoptosis. LBP inhibited the H2O2-induced down-regulation of Bcl-2 and up-regulation of Bax.

CONCLUSION: LBP could protect ARPE-19 cells from H2O2-induced apoptosis. The Bcl-2 family had relationship with the protective effects of LBP.

PMID: 25709900 [PubMed] PMCID: PMC4325234

J Ophthalmic Vis Res. 2014 Oct-Dec;9(4):494-505.

Visual prostheses: the enabling technology to give sight to the blind.

Maghami MH, Sodagar AM, Lashay A, Riazi-Esfahani H, Riazi-Esfahani M.

Abstract: Millions of patients are either slowly losing their vision or are already blind due to retinal degenerative diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD) or because of accidents or injuries. Employment of artificial means to treat extreme vision impairment has come closer to reality during the past few decades. Currently, many research groups work towards effective

solutions to restore a rudimentary sense of vision to the blind. Aside from the efforts being put on replacing damaged parts of the retina by engineered living tissues or microfabricated photoreceptor arrays, implantable electronic microsystems, referred to as visual prostheses, are also sought as promising solutions to restore vision. From a functional point of view, visual prostheses receive image information from the outside world and deliver them to the natural visual system, enabling the subject to receive a meaningful perception of the image. This paper provides an overview of technical design aspects and clinical test results of visual prostheses, highlights past and recent progress in realizing chronic high-resolution visual implants as well as some technical challenges confronted when trying to enhance the functional quality of such devices.

PMID: 25709777 [PubMed] PMCID: PMC4329712

J Ophthalmic Vis Res. 2014 Oct-Dec;9(4):487-93.

Nutrient Supplementation for Age-related Macular Degeneration, Cataract, and Dry Eye.

Hobbs RP, Bernstein PS.

Abstract: There have been enormous advances in the past decade for the treatment of age-related macular degeneration (AMD); however, these treatments are expensive and require frequent follow-up and injections which place a tremendous burden on both the healthcare system and patients. Consequently, there remains considerable interest in preventing or slowing the progression of AMD requiring treatment. Epidemiological studies have shown that diet is a modifiable AMD risk factor, and nutrient modification is a particularly appealing treatment for AMD due to the perceived universal benefit and relatively low expense. Recently, the age-related eye disease study part two (AREDS2) was concluded and demonstrated further benefit with the addition of lutein and zeaxanthin as a replacement for the β-carotene of the previous generation formulation. The addition of omega-3 essential fatty acids did not show an added benefit. This review aims to highlight some of the evidenced based body of knowledge that has been accumulated from recent studies regarding the use of nutritional supplements and their effect on AMD, cataracts, and dry eyes.

PMID: 25709776 [PubMed] PMCID: PMC4329711

Arq Bras Oftalmol. 2015 Jan-Feb;78(1):10-4.

Approach of Turkish ophthalmologists to micronutrition in age-related macular degeneration.

Ed Şahin M, Yüksel H, Şahin A, et al

PURPOSE: To evaluate the knowledge and behaviors of ophthalmologists in Turkey concerning micronutrition support in patients with age related macular degeneration (ARMD).

METHODS: This study involved 1,845 ophthalmologists. A scientific poll was sent to all participants by email. The survey covered the following: demographic features, subspecialty knowledge about micronutrition preference for prescribing micronutrition to age related macular degeneration patients, and the reason for this preference. If a participant indicated that he or she prescribed micronutrition, the participant was also asked to indicate the source of the treatment and supplemental treatments.

RESULTS: Of 1,845 ophthalmologists, 249 responded to the survey. Of the respondents, 9% (22) never, 43% (107) sometimes, 37% (92) frequently, and 11% (27) always used micronutrition. The most frequent prescribing subgroup was general ophthalmology (22%), followed by the retina-uvea subspecialty (13.9%). The micronutrition prescribing ratio was 54.8% in retina-uvea specialists when the "frequent" and "always" responses were combined. There was no statistically significant difference between subgroups with respect to prescribing micronutrition. Among the ophthalmologists prescribing micronutrition, 57.1% of them did not

use the Age-Related Eye Disease Study-1 (AREDS) criteria, and only 31.3% prescribe micronutrition according to AREDS criteria. The results for the general ophthalmologist and retina-uvea specialist subgroups were similar, 56.3% vs 20.2%, and 54.1% vs 36.1%, respectively. Micronutrition was not recommended for the following reasons: expensive (55.4%), low patient expectancy (40%), no effect (30%), and low patient drug compliance (25.4%). Moreover, 55.2% of the clinicians recommended physical activities, dietary changes, and smoking cessation; 7.3% did not recommend these behavioral changes.

CONCLUSION: This survey demonstrated that micronutrition preference in age related macular degeneration was low in ophthalmologists in Turkey. Additionally, retina specialists have a lower rate of prescribing micronutrition. Micronutrition support and behavior such as smoking cessation, dietary changes, etc. should be recommended more often to patients with age related macular degeneration.

PMID: 25714530 [PubMed - in process]