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MD Research News

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Drug treatment

Br J Ophthalmol. 2014 Jun;98 Suppl 1:i22-i27. doi: 10.1136/bjophthalmol-2013-304798.

A single-arm, investigator-initiated study of the efficacy, safety and tolerability of intravitreal aflibercept injection in subjects with exudative age-related macular degeneration, previously treated with ranibizumab or bevacizumab: 6-month interim analysis.

Singh RP, Srivastava S, Ehlers JP, Bedi R, Schachat AP, Kaiser PK.

AIM: To evaluate efficacy and safety of intravitreal aflibercept injection (IAI) in subjects who were previously treated with ranibizumab and/or bevacizumab for active exudative age-related macular degeneration (AMD).

METHODS: Patients (n=26) were enrolled in a 12-month prospective, interventional, single arm, investigator-initiated study with planned 6-month interim analysis. Patients with active exudative AMD, previously treated with ranibizumab and/or bevacizumab, were treated with 2 mg IAI every month for the first 3 months, followed by a fixed dosing schedule of 2 mg IAI every 2 months. The primary study endpoint was the mean absolute change from baseline central subfield thickness (CST) at month 12 as measured by SDOCT. Secondary outcomes included mean change from baseline best-corrected visual acuity (BCVA) score, percentage of subjects who gained or lost greater than or equal to 15 letters of vision, percentage of subjects who are 20/40 or better, percentage of subjects who are 20/200 or worse, and the incidence of adverse events (AE) and serious AEs.

RESULTS: Planned 6-month interim analysis demonstrated a mean decrease in CST of 38.6 µm ($p<0.001$) and a mean increase in ETDRS BCVA of +5.9 letters ($p<0.001$). Fifteen percent of subjects experienced a greater than 15-letter improvement in visual acuity, 84.6% of patients gained visual acuity, and no patient lost 3 lines of vision from baseline. Forty-two percent of subjects were 20/40 or better, and 11.5% of subjects were 20/200 or worse at month 6. No serious ocular or systemic AEs were encountered.

CONCLUSIONS: IAI-treated eyes demonstrated improved short-term functional and anatomic endpoints in subjects with active exudative AMD switching from previous anti-VEGF treatment when given in a fixed dosing scheme for 6 months.

PMID: 24836866 [PubMed - in process]

Ophthalmologica. 2014 May 20. [Epub ahead of print]

Detection of Antiranibizumab Antibodies among Patients with Exudative Age-Related Macular Degeneration.

Leveziel N, Pelat T, Watier H, Thullier P, Souied EH.

Purpose: The aim of this study was to detect immune responses induced by intravitreal injection (IVT) of ranibizumab in patients with exudative age-related macular degeneration (AMD) in real life conditions.

Methods: An ELISA protocol from blood samples, following 2 different steps, was used to detect antibodies directed against the variable regions of ranibizumab.

Results: Among 91 patients included, 46 received more than 10 IVTs, 36 had received 10 IVTs or fewer, and 9 were treatment naïve. Specific antiranibizumab immunoglobulins G were detected in 14/82 treated patients (17.1%). No immunization was detected among naïve patients. For patients with 10 or fewer previous IVTs, immunization against ranibizumab was detected in 4/36 patients (11.1%) whereas immunization was observed in 10/46 patients (21.7%) with more IVTs ($p = 0.20$).

Conclusions: Immunization against ranibizumab can be detected in 17% of treated patients. Further clinical studies are needed to investigate the relationship between specific immunization to anti-vascular endothelial growth factor antibodies and response or resistance to ranibizumab treatments.

PMID: 24854579 [PubMed - as supplied by publisher]

Retina. 2014 May 15. [Epub ahead of print]

REASONS FOR DISCONTINUATION OF INTRAVITREAL VASCULAR ENDOTHELIAL GROWTH FACTOR INHIBITORS IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

Vaze A, Fraser-Bell S, Gillies M.

BACKGROUND: This study was aimed to identify the reasons for discontinuing intravitreal anti-vascular endothelial growth factor therapy in neovascular age-related macular degeneration.

METHODS: This study is a retrospective chart review of a single Australian private practice analysis that included patients who discontinued treatment from March 2006 to June 2012.

RESULTS: Of 248 patients who commenced treatment, 105 (42.3%) had discontinued by June 2012. Analysis reasons for discontinuation were available for 102 of the 105 (97.1%) patients. In 9 (3.6%) patients of the entire cohort, the doctor stopped the treatment as the lesion became inactive, whereas further treatment was thought to be futile in 27 (10.9%) patients. Twenty-six (10.5%) patients declined further treatment with 2 (0.8%) because of excessive treatment visits, 2 (0.8%) because of difficulty in attending, 2 (0.8%) because of the expense, 3 (1.2%) because of pain/discomfort, 6 (2.4%) thought that the treatment was not beneficial, and 11 (4.4%) had other medical conditions that were more severe. Treatment was discontinued in 40 (16.1%) patients for other reasons such as moving to another region in 27 (10.9%) and death in 11 (4.4%).

CONCLUSION: These results indicate that the burden of intravitreal anti-vascular endothelial growth factor injections was a reason for treatment discontinuation in only a small minority of patients.

PMID: 24837049 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2014 May 6;8:847-856. eCollection 2014.

Profile of ocriplasmin and its potential in the treatment of vitreomacular adhesion.

Stefanini FR1, Maia M2, Falabella P1, Pfister M3, Niemeyer M4, Kashani AH5, Humayun MS5, Koss MJ6.

Abstract: The recent approval by the US Food and Drug Administration of ocriplasmin for the treatment of symptomatic vitreomacular adhesion (VMA), often associated with vitreomacular traction (VMT) and

macular hole (MH), has brought new attention to the field of pharmacologic vitreolysis. The need for an enzyme to split the vitreomacular interface, which is formed by a strong adhesive interaction between the posterior vitreous cortex and the internal limiting membrane, historically stems from pediatric eye surgery. This review summarizes the different anatomic classifications of posterior vitreous detachment or anomalous posterior vitreous detachment and puts these in the context of clinical pathologies commonly observed in clinical practice of the vitreoretinal specialist, such as MH, VMT, age-related macular degeneration, and diabetic macular edema. We revisit the outcome of the Phase II studies that indicated ocriplasmin was a safe and effective treatment for selected cases of symptomatic VMA and MH. Release of VMA at day 28 was achieved by 26.5% of patients in the ocriplasmin group versus 10.1% in the placebo group (P<0.001). Interestingly, for MHs, the numbers were more remarkable. Predictive factors for successful ocriplasmin treatment were identified for VMT (VMA diameter smaller than 1,500 µm) and MH (smaller than 250 µm). In comparison with the highly predictable outcome after vitrectomy, the general success rate of ocriplasmin not under clinical trial conditions has not fully met expectations and needs to be proven in real-world clinical settings. The ocriplasmin data will be compared in the future with observational data on spontaneous VMA release, will help retina specialists make more accurate predictions, and will improve outcome rates.

PMID: 24851038 [PubMed - as supplied by publisher]

Eur J Ophthalmol. 2014 May 20:0. doi: 10.5301/ejo.5000486. [Epub ahead of print]

Bevacizumab treatment for choroidal neovascularization associated with adult-onset foveomacular vitelliform dystrophy.

Tiosano L, Jaouni T, Averbukh E, Grunin M, Banin E, Chowers I.

PURPOSE: To evaluate choroidal neovascularization (CNV) associated with adult-onset foveomacular vitelliform dystrophy (AOFVD) and its response to bevacizumab therapy.

METHODS: Demographics, clinical characteristics, response to bevacizumab therapy, and central foveal thickness (CFT) were retrospectively assessed in 11 eyes with CNV associated with AOFVD. Sixty consecutive patients with neovascular age-related macular degeneration (AMD) were compared to the patients with AOFVD for all clinical characteristics and responses evaluated.

RESULTS: The mean (±SD) initial logMAR visual acuity (0.7 ± 0.8 vs. 1 ± 0.75), age at onset, number of bevacizumab injections (12.4 ± 10.4 vs 9 ± 6.7), and final logMAR visual acuity (0.87 ± 0.7 vs 1 ± 0.85) were similar between AOFVD and AMD. The mean CFT in AOFVD was reduced from 418 ± 144 µm to 330 ± 64 µm following treatment (p = 0.03). At the final examination, visual acuity had improved in 3 eyes, stabilized in 1 eye, and was reduced in 7 of the AOFVD eyes examined.

CONCLUSIONS: Bevacizumab therapy for AOFVD-associated CNV resulted in reduced foveal thickness, but a guarded visual outcome was still found, due to progression of the vitelliform lesions.

PMID: 24846624 [PubMed - as supplied by publisher]

Ophthalmologe. 2014 May;111(5):438-42. doi: 10.1007/s00347-013-2922-y.

[Health services for patients with neovascular age-related macular degeneration in Germany]. [Article in German]

Finger RP, Holz FG.

Abstract: In neovascular age-related macular degeneration (NVAMD) successful treatment outcome depends on regular intravitreal injections of vascular endothelial growth factor inhibitors (anti-VEGF). Several observational trials on the use of ranibizumab in the clinical routine demonstrated a low injection frequency, a low number of ophthalmic reviews which included optical coherence tomography, and

suboptimal treatment outcomes in Germany. To date it remains unclear whether the use of ranibizumab reflects the use of all anti-VEGF agents including aflibercept and bevacizumab in the clinical routine in Germany. However, based on available data, treatment provision and outcomes seem to be suboptimal, in particular for elderly patients with NVAMD. As poorly treated NVAMD carries a high risk of loss of vision and ultimately blindness, service provision and treatment outcomes need to be improved.

PMID: 24838864 [PubMed - in process]

Other treatment & diagnosis

Am J Ophthalmol. 2014 May 17. pii: S0002-9394(14)00241-4. doi: 10.1016/j.ajo.2014.05.007. [Epub ahead of print]

Evaluation of Choroidal Neovascularization with Indocyanine Green Angiography in Neovascular Age-related Macular Degeneration Subjects Undergoing Intravitreal Bevacizumab Therapy.

Rush RB, Rush SW, Aragon AV 2nd, Ysasaga JE.

PURPOSE: To report the clinical implications of interval changes in choroidal neovascularization (CNV) size measured by indocyanine green (ICG) angiography in neovascular age-related macular degeneration (AMD) patients undergoing intravitreal bevacizumab therapy.

DESIGN: Retrospective, consecutive chart review METHODS: The charts of neovascular AMD patients that underwent intravitreal bevacizumab therapy using a treat-and-extend dosing schedule were reviewed. ICG angiographic CNV surface areas were measured at baseline, 2 months, 6 months, and 12 months in each subject. The primary outcome was change in CNV size. Secondary outcomes included the correlation of change in CNV surface area with change in best-corrected visual acuity (BCVA), change in central macular thickness on optical coherence tomography (OCT), and the number of injections delivered over the 12-month study interval.

RESULTS: 123 subjects were included in the analysis. The baseline CNV size was 1.9 mm2 +/-2.5 mm2. CNV size was 1.66 mm2 +/-2.11 mm2 at 2 months, 1.60 mm2 +/-2.23 mm2 at 6 months, and 1.50 mm2 +/-2.12 mm2 at 12 months. The change in CNV size from baseline was not statistically significant at any of the follow-up intervals. A decrease in CNV size of 33% or more at 2 months was associated with a significant decrease in CNV size at 12 months (p=0.0096), complete resolution of CNV at 12 months (p=0.0013), and a decrease in the number of injections delivered over the study interval (p=0.0165). Complete resolution of CNV at 12 months occurred in 7.3% of subjects. Subjects that had complete resolution of CNV at 12 months were significantly more likely to gain 3 more lines of BCVA at the end of the study interval (p=0.0131). No significant correlation was found between CNV size and change in central macular thickness on OCT.

CONCLUSIONS: Our study suggests that change in CNV size on ICG angiography may help the clinician predict the clinical course of neovascular AMD subjects undergoing intravitreal bevacizumab therapy using a treat-and-extend dosing schedule.

PMID: 24844972 [PubMed - as supplied by publisher]

Saudi J Ophthalmol. 2014 Apr;28(2):129-33. doi: 10.1016/j.sjopt.2014.03.001. Epub 2014 Mar 12.

Retention of good visual acuity in eyes with neovascular age-related macular degeneration and chronic refractory subfoveal subretinal fluid.

Bhavsar KV, Freund KB.

PURPOSE: To describe the clinical characteristics of a subset of eyes with neovascular age-related macular degeneration (NVAMD) receiving intravitreal anti-vascular endothelial growth factor (anti-VEGF)

therapy which retain good visual acuity despite chronic, persistent subfoveal subretinal fluid (SRF).

DESIGN: Retrospective, observational case series.

METHODS: Study eyes were identified from a consecutive series of 186 patients treated with anti-VEGF therapy seen for regular follow-up over a 3-month period. The clinical histories of 10 eyes of 9 patients with NVAMD, chronic subfoveal SRF despite continuous anti-VEGF therapy, and good long-term visual acuity of 20/40 or greater were reviewed. Demographic factors, baseline and final visual acuity, neovascular lesion type, duration of persistent fluid, baseline and final subfoveal choroidal thickness, presence of geographic atrophy, and number of anti-VEGF injections were analyzed.

RESULTS: The mean age of patients was 78 years (range 55-91). The mean duration of persistent fluid was 5.2 years (range 1.3-11.0). Long-term visual acuities remained stable at 20/40 or better in all eyes. All eyes had type 1 (sub-retinal pigment epithelial) neovascularization. Average baseline subfoveal choroidal thickness was 285.3 μm and the average follow-up subfoveal choroidal thickness was 239.7 μm. No eyes had the presence of geographic atrophy. The mean number of injections was 36.5 (range 17-66).

CONCLUSION: Some eyes with type 1 neovascularization associated with chronic persistent subfoveal subretinal fluid despite continuous intravitreal anti-VEGF therapy may maintain good long-term visual outcomes. We hypothesize that type 1 neovascularization and greater subfoveal choroidal thickness may exert a protective effect on photoreceptor integrity. Further studies are necessary to assess long-term visual prognosis and predictive factors in patients with type 1 neovascularization leading to persistent subretinal fluid that is recalcitrant to anti-VEGF treatment.

PMID: 24843306 [PubMed] PMCID: PMC4023102

Med Hypotheses. 2014 May 9. pii: S0306-9877(14)00193-5. doi: 10.1016/j.mehy.2014.04.031. [Epub ahead of print]

Applying theories and interventions from behavioral medicine to understand and reduce visual field variability in patients with vision loss.

Rozanski C, Haythornthwaite JA, Dagnelie G, Bittner AK.

Abstract: Visual field (VF) test results are often unreliable in visually impaired patients, but continue to be a cornerstone of clinical trials and play a vital role in clinical decision making since they are the primary method to determine patients' functional vision loss or progression. Currently, patients are typically asked to perform VF tasks with minimal instruction or consideration of their psychological experience during the test. The gradual loss of vision due to retinal diseases, such as retinitis pigmentosa (RP), age-related macular degeneration (AMD), or glaucoma can contribute to the experience of negative psychosocial states, such as anxiety, stress, and depression, as well as diminished quality of life. We hypothesize that VF testing elicits test performance anxiety and perception of functional losses of vision, which induces distracting negative thoughts that result in increased VF test variability. Resources for processing and responding to vision-related information may be diverted from task-relevant VF stimuli to task-irrelevant ones, such as internal worry and test anxiety, thereby resulting in VF test performance decrements. We present a theoretical model to support the hypothesis that VF variability is linked to patients' negative thoughts during VF testing. This conceptual framework provides a basis for the development of coping strategies and mindfulness-based interventions to be evaluated in future research aimed at improving psychosocial states and VF reliability in visually-impaired patients. It would be highly significant to intervene by modifying negative thoughts during VF testing to reduce test variability in glaucoma patients who are progressively losing vision to a blinding eye disease, but whose vision loss has not been accurately identified and treated early enough due to variable VF results. In clinical trials of potential interventions for RP and non-neovascular AMD, reducing VF variability would effectively increase the precision for detecting treatment effects and allow a reduction in the number of VF tests needed to estimate the treatment responses, thus reducing burden on investigators and patients, as well as saving time and money.

PMID: 24854574 [PubMed - as supplied by publisher]

Retina. 2014 Jun;34(6):1046-54. doi: 10.1097/IAE.0000000000000237.

PRESBYOPIA-CORRECTING INTRAOCULAR LENSES AND CORNEAL REFRACTIVE PROCEDURES: A Review for Retinal Surgeons.

Ahmad BU, Shah GK, Hardten DR.

PURPOSE: To review the specific challenges and pitfalls that vitreoretinal surgeons may face when operating on eyes with presbyopia-correcting intraocular lenses or previous corneal refractive surgery. In addition, this review aims to familiarize vitreoretinal surgeons with specifications of currently available Food and Drug Administration-approved presbyopia-correcting intraocular lenses.

METHODS: Review of current literature performed with PubMed for search terms "presbyopia," "correction," "IOL," "vitreoretinal," "challenges," and "surgical" both singly and in combination as well as closely related terms.

RESULTS AND CONCLUSION: Specific intraoperative issues with presbyopia-correcting intraocular lenses that may be encountered include peripheral visualization, condensation, lens material issues particularly with silicone oil, decentration, Z-syndrome, and foveal image displacement. Every patient undergoing retinal surgery should also be asked about previous laser-assisted in situ keratomileusis/photorefractive keratectomy because those eyes require special attention to surface hydration and care to avoid epithelial removal if possible. Intracorneal ring segments and corneal inlays can cause effects similar to those of a small pupil. However, these can be managed with thorough preoperative evaluation and various intraoperative maneuvers. In addition, retinal physicians should be aware that macular disorders, such as age-related macular degeneration, may be exacerbated by potential loss of contrast sensitivity.

PMID: 24849701 [PubMed - in process]

Ophthalmology. 2014 May 15. pii: S0161-6420(14)00367-4. doi: 10.1016/j.ophtha.2014.04.020. [Epub ahead of print]

Comparison of Optical Coherence Tomography Assessments in the Comparison of Age-Related Macular Degeneration Treatments Trials.

Folgar FA, Jaffe GJ, Ying GS, Maguire MG, Toth CA; Comparison of Age-Related Macular Degeneration Treatments Trials Research Group.

OBJECTIVE: To determine agreement between spectral-domain (SD) and time-domain (TD) optical coherence tomography (OCT) image assessments by certified readers in eyes treated for neovascular age-related macular degeneration (AMD).

DESIGN: Cross-sectional study within the Comparison of AMD Treatments Trials (CATT).

PARTICIPANTS: During year 2 of CATT, 1213 pairs of SD OCT and TD OCT scans were compared from a subset of 384 eyes.

METHODS: Masked readers independently graded OCT scans for presence of intraretinal fluid (IRF), subretinal fluid (SRF), and sub-retinal pigment epithelium (RPE) fluid and performed manual measurements of retinal, SRF, and subretinal tissue complex thicknesses at the foveal center.

MAIN OUTCOME MEASURES: Presence of fluid was evaluated with percent agreement, κ coefficients with 95% confidence intervals (CIs), and McNemar tests. Thickness measurements were evaluated with mean difference (Δ) ±95% limits of agreement and intraclass correlation coefficients (ICCs) with 95% CIs.

RESULTS: Between SD OCT and TD OCT, agreement on presence of any fluid was 82% (κ = 0.46; 95% CI, 0.40-0.52), with 5% more SD OCT scans demonstrating fluid (P<0.001). Agreement on presence of SRF was 87% and sub-RPE fluid was 80%, with more SD OCT scans demonstrating fluid (both P < 0.001). Agreement on IRF was 73% (κ = 0.47; 95% CI, 0.42-0.52), with 6% more TD OCT scans demonstrating

fluid (P < 0.001). Between SD OCT and TD OCT, mean thickness of the retina was Δ = 5±67 μm, SRF was Δ = 1.5±35 μm, and subretinal tissue complex was Δ = 5±86 μm. Thickness measurements were reproducible for retina (ICC = 0.84; 95% CI, 0.83-0.86), SRF (ICC = 0.88; 95% CI, 0.86-0.89), and subretinal tissue complex (ICC = 0.91; 95% CI, 0.89-0.92), with ≤25-μm difference in these measurements in 71%, 94%, and 61% of paired scans, respectively.

CONCLUSIONS: Agreement on fluid presence and manual thickness measurements between paired scans from each OCT modality was moderate, providing a reasonable basis to compare CATT results with future SD OCT-based trials. Fluid was detected 5% more frequently with SD OCT, which may increase frequency of fluid-based treatment. Lower-resolution and artifactual interpretation of dark areas as cystoid edema may explain the greater frequency of IRF detected with TD OCT.

PMID: 24835760 [PubMed - as supplied by publisher]

Eur J Ophthalmol. 2014 May 17:0. doi: 10.5301/ejo.5000483. [Epub ahead of print]

Prevalence and clinical characteristics of Charles Bonnet syndrome in Madrid, Spain.

Santos-Bueso E, Sáenz-Francés F, Serrador-García M, Porta-Etessam J, Martínez-de-la-Casa JM, García-Feijoo J, García-Sánchez J.

PURPOSE: Charles Bonnet syndrome (CBS) is a condition characterized by development of visual hallucinations in patients with no cognitive impairment and significant loss of vision mainly caused by age-related macular degeneration (AMD) or glaucoma.

METHODS: This was a study of prevalence and characteristics of CBS diagnosed at the Neuroophthalmic Unit within the Ophthalmology Department of Hospital Clínico San Carlos (HCSC), Madrid, Spain.

RESULTS: The CBS prevalence in patients from HCSC Madrid is 0.47%, rising to 15% in patients with low vision. Women over 80 years of age comprised 58.3% of the patients, who mainly had AMD (58.3%). Main characteristics of hallucinations included animals (50%), color (58.3%), moving (75%), 6- to 12-month evolution (50%), three times a day frequency (75%), and 3- to 5-minute duration (50%).

CONCLUSIONS: Charles Bonnet syndrome is a complex process that must be treated jointly by ophthalmologists, neurologists, and psychiatrists in order to ensure accurate diagnosis and adequate management. New studies are needed in order to improve awareness of clinical manifestation of this condition, the incidence of which is underestimated due to patients' fear of being branded mentally ill, as well as physicians' lack of knowledge about CBS.

PMID: 24846623 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2014 May 19;55(5):3149. doi: 10.1167/iovs.14-14569.

Author response: additional considerations in the utility of dark adaptometry for the diagnosis of age-related macular degeneration.

Jackson GR, Scott IU, Kim IK, Quillen DA, Iannaccone A, Edwards JG.

PMID: 24840311 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2014 May 19;55(5):3148. doi: 10.1167/iovs.14-14317.

Additional considerations in the utility of dark adaptometry for the diagnosis of age-related macular degeneration.

VanderBeek BL.

PMID: 24840310

Pathogenesis

Invest Ophthalmol Vis Sci. 2014 May 20. pii: IOVS-13-13732. doi: 10.1167/iovs.13-13732. [Epub ahead of print]

Fullerenol Protects Retinal Pigment Epithelial Cells from Oxidative Stress-Induced Premature Senescence via Activating SIRT1.

ZhuGe CC, Xu JY, Zhang J, Li W, Li P, Li Z, Chen L, Liu X, Shang P, Xu H, Lu YJ, Wang F, Lu L, Xu GT.

Abstract: Oxidative stress-induced retinal pigment epithelium (RPE) senescence is one of the important pathogenesis factors of age-related macular degeneration (AMD). This study aimed to develop a new anti-senescence based intervention and clarify its mechanism. Cell premature senescence model was established in porcine primary RPE cells and ARPE-19 cells by exposuring the cells to pulsed H2O2 stress for 5 days, and confirmed with SA-β-gal Staining. The Fullerenol (Fol) concentration in the medium was 50 ng/ml. The cellular redox status was determined by cellular ROS staining, catalase activity, and the GSH/GSSG ratio respectively. DNA double-strand breaks were determined by γH2AX quantitative analysis. Cell cycle analysis was performed with the Flow Cytometry. SIRT1 activity was examined with SIRT1 Assay Kit. SIRT1 expression in ARPE-19 Cells were modified with lentiviral-mediated infection. RESULTS. Pulsed H2O2 exposure triggered the K382 p53 acetylation and increase of p21Waf1. It also increased γH2AX foci accumulation and phosphor-ATM level in RPE cells. Fullerenol protected the RPE cells, as it reduced the number of positive SA-β-gal staining cell, alleviated the cellular antioxidants depletion and reduced genomic DNA damage. Its mechanism involve the SIRT1 activation, resulting in the acetyl-p53 and p21Waf1 decrease. The SIRT1 role in protecting cells in response to Fullerenol were confirmed by SIRT1 activator (Resveratrol) and inhibitors (Nicotinamide and Sirtinol), and through SIRT1 gene modification. Fullerenol rescues RPE cells from oxidative stress-induced senescence through anti-oxidation activity and SIRT1 activation. The Fullerenol's protection is useful for the development of new strategies to treat oxidative stress related retinal diseases like AMD etc.

PMID: 4845634 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2014 May 22. pii: IOVS-14-14502. doi: 10.1167/iovs.14-14502. [Epub ahead of print]

Associations between Abnormal Rod-Mediated Dark Adaptation and Health and Functioning in Older Adults with Normal Macular Health.

Owsley C, Huisingh C, Jackson GR, Curcio CA, Szalai AJ, Dashti N, Clark ME, Rookard K, McCrory MA, Wright TT, Callahan MA, Kline LB, Witherspoon CD, McGwin G Jr.

Purpose: Delayed rod-mediated dark adaptation (DA) is characteristic of early age-related macular degeneration (AMD) and can also be observed in some older adults in normal macular health. Here we examine cross-sectional associations between rod-mediated DA and risk factors for AMD in older adults in normal macular health.

Methods: The sample consisted of adults aged ≥ 60 years old in normal macular health per grading of fundus photos using an established disease classification system. Rod-mediated DA was psychophysically measured following a photobleach using a computer-automated dark adaptometer with targets centered at 5° on the inferior vertical meridian. The speed of DA was characterized by the rod-intercept value, with abnormal DA defined as rod-intercept ≥ 12.3 minutes. We assessed several health and functional characteristics that the literature has suggested increase AMD risk (e.g., smoking, alcohol use,

inflammatory markers, apolipoproteins, low luminance visual acuity, chronic medical conditions, body mass, family history).

Results: Among 381 participants (mean age 68.5 years, SD 5.5), 78% had normal and 22% had abnormal DA, with the prevalence of abnormal DA increasing with age. After age-adjustment, abnormal DA was associated with increased odds of elevated C-reactive protein (CRP), heavy use of or abstention from alcohol, high blood pressure, and drop in visual acuity under mesopic conditions.

Conclusions: Despite having normal macular health according to accepted definitions of AMD presence, about 1/4 of older adults recruited from primary eye care clinics had abnormal DA, which was associated with known risk factors for AMD including elevated CRP.

PMID: 24854857 [PubMed - as supplied by publisher]

Inflamm Allergy Drug Targets. 2014 May 22. [Epub ahead of print]

Inflammaging in Skin and other Tissues - the Roles of Complement System and Macrophage.

Zhuang Y, Lyga J.

Abstract: Inflammaging refers to a continuous, low-grade inflammation associated with aging. Such chronic inflammatory response could build up with time and gradually cause tissue damage. It is considered one of the driving forces for many age-related diseases such as diabetes, atherosclerosis, age-related macular degeneration (AMD), and skin aging. There is mounting evidence that indicates aging is driven by the pro-inflammatory cytokines and substances produced by our body's innate immune system. The macrophage and complement system, two important components of innate immune system, have attracted more and more attention since they appear to be involved in pathogenesis of several inflammaging-associated diseases, such as AMD and atherosclerosis. This paper will review what we know about these two innate immune systems in the pathogenesis of AMD, atherosclerosis and skin aging.

PMID: 24853681 [PubMed - as supplied by publisher]

Epidemiology

Am J Ophthalmol. 2014 May 17. pii: S0002-9394(14)00238-4. doi: 10.1016/j.ajo.2014.05.004. [Epub ahead of print]

Comparison of Exudative Age-related Macular Degeneration Subtypes in Japanese and French Patients: Multi-center diagnosis with multimodal imaging.

Coscas G, Yamashiro K, Coscas F, De Benedetto U, Tsujikawa A, Miyake M, Gemmy Cheung CM, Wong TY, Yoshimura N.

PURPOSE: To compare and analyze differences and similarities between Japanese and French patients in subtype diagnosis of exudative age-related macular degeneration (AMD) as determined by fundus photography (FP) and fluorescein angiography (FA), and a multimodal imaging involving FP, FA, indocyanine green angiography (ICGA), and optical coherence tomography (OCT).

DESIGN: Retrospective chart review.

METHODS: We determined the subtype diagnosis for 99 consecutive Japanese eyes and 94 consecutive French eyes with exudative AMD. The first-step diagnosis was made using FP and FA, while the second-step diagnosis was made using FP, FA/ICGA, and OCT. The diagnoses made by Japanese and French physicians were compared, and when the diagnoses differed, a third Institute was consulted to arrive at a final consensus and diagnosis.

RESULTS: The first-step diagnosis showed 20-30% disagreement against the final diagnosis, but the second-step diagnosis showed only 10% disagreement. Polyopidal choroidal vasculopathy (PCV) was observed more in Japanese (48%) than in French (9%), and the rate of PCV with type 1 or 2 choroidal neovascularization (CNV) was extremely low: 3% in Japanese and 0% in French. Type 1 CNV was found significantly more in French cases (53.3% vs. 35.1%, P = 0.018), while the rate of eyes with type 2 CNV only or chorioretinal anastomosis was similar between populations.

CONCLUSIONS: Multimodality imaging significantly improved the sub-classification of AMD. There were significant differences between the 2 series in the proportions of type 1 CNV and PCV, while the proportions of type 2 CNV only and chorioretinal anastomosis were similar between groups.

PMID: 24844973 [PubMed - as supplied by publisher]

Genetics

Acta Ophthalmol. 2014 May 22. doi: 10.1111/aos.12437. [Epub ahead of print]

Environmental and genetic risk factors for retinal angiomatous proliferation.

Caramoy A, Ristau T, Lechanteur YT, Ersoy L, Müller S, Gelisken F, Hoyng CB, Kirchhof B, den Hollander AI, Fauser S.

PURPOSE: To identify genetic and environmental risk factors in patients with retinal angiomatous proliferation (RAP), a clinical subtype of age-related macular degeneration (AMD).

METHODS: In this case-control study, 108 AMD cases with RAP, 258 AMD patients with choroidal neovascularization (CNV) without RAP and 443 healthy controls were evaluated. Single nucleotide polymorphisms in age-related maculopathy susceptibility 2 (ARMS2) and complement factor H (CFH) and various environmental risk factors were analysed. Statistical analysis was performed by univariate and multivariate regression analysis.

RESULTS: High age, female sex and genetic variants in CFH and ARMS2 were identified as risk factors for developing any CNV. In RAP patients, arterial hypertension was also identified as a risk factor (OR 2.39; p = 0.0005). Compared with the 'non-RAP' CNV group, the association with high age (OR 1.05; p = 0.008) and arterial hypertension (OR 1.82; p = 0.02) was significantly higher in RAP patients, while the association with CFH risk alleles (homozygous OR 0.40; p = 0.003) was significantly lower, which was confirmed in a multivariate analysis (OR 0.41; p = 0.03 for the heterozygous risk allele and OR 0.38; p = 0.03 for the homozygous risk allele).

CONCLUSION: The association with the CFH Y402 risk allele was less pronounced in RAP patients than in 'non-RAP' CNV patients, while the association with high age and arterial hypertension appeared to be stronger. These findings stress the importance of detailed phenotyping in AMD to identify homogeneous AMD subtypes and their different risk factors and disease mechanisms.

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Whole -exome sequencing identifies rare, functional CFH variants in families with macular degeneration.

Yu Y, Triebwasser MP, Wong EK, Schramm EC, Thomas B, Reynolds R, Mardis E, Atkinson JP, Daly M, Raychaudhuri S, Kavanagh D, Seddon JM.

Abstract: We sequenced the whole exome of 35 cases and 7 controls from 9 age-related macular degeneration (AMD) families in whom known common genetic risk alleles could not explain their high disease burden and/or their early-onset advanced disease. Two families harbored novel rare mutations in CFH (R53C and D90G). R53C segregates perfectly with AMD in 11 cases (heterozygous) and 1 elderly

control (reference allele) (LOD=5.07, P=6.7x10-7). In an independent cohort, 4 out of 1,676 cases but none of the 745 examined controls or the 4300 NHBLI ESP samples carried the R53C mutation (P=0.0039). In another family of 6 siblings, D90G similarly segregated with AMD in 5 cases and 1 control (LOD=1.22, P=0.009). No other sample in our large cohort or the ESP had this mutation. Functional studies demonstrated that R53C decreased the ability of FH to perform decay accelerating activity. D90G exhibited a decrease in cofactor-mediated inactivation. Both of these changes would lead to a loss of regulatory activity, resulting in excessive alternative pathway activation. This study represents an initial application of the whole-exome strategy to families with early-onset AMD. It successfully identified high impact alleles leading to clearer functional insight into AMD etiopathogenesis.

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Diet & lifestyle

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[A survey of vision-related quality of life in patients with exudative age-related macular degeneration].[Article in Chinese]

Zhu W, Ren X, Yang X, Zhou H, Yu J, Xu J, Liu N.

OBJECTIVE: To evaluate the vision-related quality of life in patients with exudative age-related macular degeneration (AMD).

METHODS: Retrospective case-series study.One hundred and twenty-two patients with exudative AMD who were treated in Beijing Tongren Eye Center from July 2007 to July 2008 were invited to participate in this study.Vision-related quality of life was evaluated by the 25-item National Eye Institute Visual Functioning Questionnaire.Statistical analysis was performed using t test for data which were normal distribution and using Wilcoxon rank sum test for data which were abnormal distribution.

RESULTS: Eighty-seven cases were fully completed and included in the final analysis within the 122 questionnaires. The total score of the questionnaire was 57.2 ± 18.4, excluded driving item. The lowest scoring item was near activities with mean score of 30.8 ± 22.3. There was statistically significant difference in mental health between male (52.9 ± 26.3) and female (40.8 ± 26.0) (w = 1 175, P < 0.05). Except for the general health and ocular pain, patients with binocular involvement showed statistically significant lower scores than those with monocular involvement in all other subscales (P < 0.05). The two age groups (patients <65 vs. ≥ 65 years old) in binocular involvement group showed statistically significant difference only in the subscale of social activities (56.6 ± 22.2 vs.42.3 ± 30.2) (w = 97, P = 0.013).

CONCLUSIONS: This study suggests that exudative AMD damaged patients'near activities seriously.Female patients tends to have lower scores than male in mental health. The score of patients with binocular involvement is lower than that of patients with monocular involvement. Age has significant effects on the social activities of those patients with binocular involvement.

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