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Drug treatment

Ophthalmology. 2016 Jan 28. [Epub ahead of print]

Intravitreal Aflibercept Injection in Diabetic Macular Edema Patients with and without Prior Anti-Vascular Endothelial Growth Factor Treatment: Outcomes from the Phase 3 Program.

Do DV, Nguyen QD, Vitti R, Berliner AJ, Gibson A, Saroj N, Soo Y, Boyer DS.

PURPOSE: To evaluate visual and anatomic outcomes after intravitreal aflibercept injection (IAI) versus laser in diabetic macular edema (DME) patients with and without prior anti-vascular endothelial growth factor (VEGF) treatment for DME.

DESIGN: Post hoc analysis of eyes from 2 similarly designed, phase 3 trials, VISTA and VIVID.

PARTICIPANTS: Patients (eyes) with DME with central involvement from VISTA (n = 461) and VIVID (n = 404).

METHODS: Eyes received IAI 2 mg every 4 weeks (2q4), IAI 2 mg every 8 weeks after 5 monthly doses (2q8), or macular laser photocoagulation.

MAIN OUTCOME MEASURES: This study reports exploratory outcomes through week 100. Analyses focused on VISTA because more patients received prior anti-VEGF therapy in VISTA (42.9%) versus VIVID (8.9%).

RESULTS: Of 42.9% of patients in VISTA who received prior anti-VEGF treatment, 83.3% to 92.6% received ≥ 1 prior injections of bevacizumab, and 71.4% to 82.4% received bevacizumab only as prior anti-VEGF treatment for a duration ranging from 28 days to 3.9 years. In patients with prior anti-VEGF treatment, mean best-corrected visual acuity (BCVA) changes from baseline in the IAI 2q4, IAI 2q8, and laser groups were +10.4 letters, +10.5 letters, and -0.7 letters at week 52 and +10.9 letters, +10.8 letters, and -0.8 letters at week 100, respectively. Corresponding changes in patients without prior anti-VEGF treatment were +14.1 letters, +11.0 letters, and +0.9 letters at week 52 and +12.0 letters, +11.3 letters, and +2.1 letters at week 100. In patients with prior anti-VEGF treatment, mean reductions in central retinal thickness were 180.2 μm , 192.2 μm , and 90.9 μm at week 52 and 180.1 μm , 196.4 μm , and 94.1 μm at week 100. Corresponding reductions in patients without prior anti-VEGF treatment were 190.3 μm , 175.7 μm , and 61.0 μm at week 52 and 200.0 μm , 186.7 μm , and 76.9 μm at week 100. The most frequent serious ocular adverse event was vitreous hemorrhage (1.3%, 0.7%, and 1.9%, respectively).

CONCLUSIONS: Visual and anatomic improvements over laser with both IAI regimens were significant and similar through week 100 in subgroups of patients in VISTA with and without prior anti-VEGF treatment for DME.

PMID: 26832658 [PubMed - as supplied by publisher]

Eur J Ophthalmol. 2016 Feb 3:0. [Epub ahead of print]

Comparison of choroidal thickness changes following intravitreal dexamethasone, ranibizumab, and triamcinolone in eyes with retinal vein occlusion.

Yumusak E, Ornek K, Dikel NH.

PURPOSE: To evaluate short-term choroidal thickness changes following intravitreal dexamethasone implant (DEX), ranibizumab (RAN), and triamcinolone acetonide (TA) in eyes with retinal vein occlusion (RVO) and macular edema (ME).

METHODS: In this prospective study, 35 eyes of 35 patients with RVO and ME who were treated with intravitreal injections of DEX, RAN, and TA were included. Choroidal thickness was measured using semiautomated segmentation of enhanced depth imaging with optical coherence tomography at fovea and parafoveal areas. Changes in choroidal thickness following treatment were compared statistically.

RESULTS: Choroidal thickness decreased following DEX, RAN, and TA treatments (all $p < 0.05$). In the DEX group, at the first month nasal 1,500 μm (N11,500) and at the third month subfoveal (SF3) and nasal 500 μm (N3500) choroidal thickness revealed a significant reduction compared to RAN and TA groups (all $p < 0.05$). In the TA group, choroidal thickness showed a significant reduction only at nasal 1,500 μm (N31,500) at the third month ($p < 0.05$).

CONCLUSIONS: Choroidal thickness was decreased in all 3 groups. The DEX and TA groups showed a significant reduction at some areas. Ranibizumab had the smallest effect on choroidal thickness after 3 months among all groups.

PMID: 26847213 [PubMed - as supplied by publisher]

Retina. 2016 Feb 2. [Epub ahead of print]

UNTREATED OBSTRUCTIVE SLEEP APNEA HINDERS RESPONSE TO BEVACIZUMAB IN AGE-RELATED MACULAR DEGENERATION.

Schaal S, Sherman MP, Nesmith B, Barak Y.

PURPOSE: To compare functional and anatomical responses to intravitreal bevacizumab in patients with exudative age-related macular degeneration (AMD) between two groups of patients with obstructive sleep apnea (OSA) with and without treatment with continuous positive airway pressure therapy.

METHODS: Patients with OSA were categorized into 2 groups: 18 untreated and 20 treated with continuous positive airway pressure therapy. All patients had exudative AMD and received treatment with intravitreal bevacizumab. Central retinal thickness was plotted against time to assess anatomical response. Logarithm of the minimum angle of resolution visual acuity changes determined functional effect. Total number of intravitreal injections administered was assessed.

RESULTS: Treated OSA group received 8 ± 7 total injections; untreated OSA group received 16 ± 4 injections ($P < 0.05$). Treated OSA group achieved statistically significant better visual acuity (logarithm of the minimum angle of resolution, 0.3 ± 0.24 , 20/40), as opposed to the untreated group (logarithm of the minimum angle of resolution, 0.7 ± 0.41 ; $P < 0.05$). Central retinal thickness improved in the treated OSA group compared with the untreated group: $358 \pm 95 \mu\text{m}$ to $254 \pm 45 \mu\text{m}$ and $350 \pm 75 \mu\text{m}$ to $322 \pm 105 \mu\text{m}$, respectively ($P < 0.05$, 20/100).

CONCLUSION: Untreated OSA hinders the response of exudative AMD to intravitreal bevacizumab. Treatment of OSA with continuous positive airway pressure therapy yields a subsequent anatomical response and functional improvement while requiring significantly less injections. Identifying and treating underlying OSA earlier in patients with exudative AMD may yield better functional outcomes.

PMID: 26841211 [PubMed - as supplied by publisher]

Zhonghua Yan Ke Za Zhi. 2015 Nov;51(11):818-821.

[Clinical observation of a new anti-VEGF drugs conbercept for wet age-related macular degeneration].[Article in Chinese]

Lu H, Cui J, Dong H, Luo B, Xiu W, Li H.

OBJECTIVE: To observe the efficacy and safety of intravitreal injection of conbercept, a new drugs of VEGFR fusion proteins, on wet age-related macular degeneration (wAMD).

METHODS: To analyze retrospectively the clinical data of 58 patients with wet wAMD, which was diagnosed by examination of ETDRS charts, color fundus photograph, fluorescein angiography (FFA) and optical coherence tomography (OCT), were underwent intravitreal injection conbercept 0.5 mg (0.05 ml of 10 g/L). Follow-up time was 6 to 12 months. Visual acuity (ETDRS charts letter), retinal thickness, leakage of CNV and operative complications before and after the treatment were analyzed.

RESULTS: Conbercept injection therapeutic times were 3-5, the average therapeutic times were 3.05. At the end of the follow-up period, the mean letter of ETDRS charts was 50.20 ± 12.87 , increased 26.20 letters ($t=2.936$, $P<0.01$). the ETDRS charts improved 15 or more letters in 33 eyes (53.23%), decreased more than 15 letters in 2 eyes (3.23%); the average foveal thickness on OCT images were (223 ± 74) μ m after treatment, decreased significantly ($t=3.669$, $P<0.01$) ; FFA showed CNV complete closure in 34 eyes (54.84%), partial closure in 23 eyes (37.10%), no change in 5 eyes (8.06%). IOP increased in 2 eyes after treatment and recovered within one week.

CONCLUSIONS: Intravitreal injection of conbercept for wAMD was well tolerated, with an improvement in BCVA, macular edema and leakage of CNV, reduce the risk of rehaemorrhagia.

PMID: 26850582 [PubMed - as supplied by publisher]

Ocul Immunol Inflamm. 2016 Jan 30;1-4. [Epub ahead of print]

Evaluation of Aqueous Flare Levels Following Intravitreal Ranibizumab Injection for Neovascular Age-related Macular Degeneration.

Uzun A, Yalcindag FN, Demirel S, Batýođlu F, Ozmert E.

PURPOSE: To evaluate aqueous flare levels following intravitreal ranibizumab injection for neovascular age-related macular degeneration (AMD).

METHODS: In total, 81 eyes of 79 patients who underwent intravitreal ranibizumab injection for neovascular AMD were included. Aqueous flare was evaluated before pupillary dilatation with Kowa FM-600 laser flare meter at baseline, and 1 day, and 1 month after intravitreal administration of ranibizumab 0.5 mg (0.05 mL).

RESULTS: The mean anterior chamber flare was 10.7 ± 6.8 (range: 1.5-35.4) ph/ms before the injection, 12.5 ± 8.9 (range: 0.3-43) ph/ms on the first day, and 9.9 ± 5.7 (range: 0.2-28.4) ph/ms in the first month. On the first day, a subtle increasing of flare was observed. However, the difference between the mean aqueous flare levels at baseline and postoperative first day and first month was not statistically different ($p>0.05$).

CONCLUSIONS: No significant short-term intraocular inflammation was noted in these eyes receiving ranibizumab for the treatment of neovascular AMD.

PMID: 26828124 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2016 Jan 13;10:87-96. eCollection 2016.

A retrospective study of the real-life utilization and effectiveness of ranibizumab therapy for neovascular age-related macular degeneration in the UK.

Hykin P, Chakravarthy U, Lotery A, McKibbin M, Napier J, Sivaprasad S.

PURPOSE: AURA was an international, retrospective, observational study that monitored the real-life use and effectiveness of ranibizumab injections in patients with neovascular age-related macular degeneration (nAMD). This paper reports the findings from the UK.

METHODS: Patients who started treatment with ranibizumab between January 1, 2009, and August 31, 2009, and had documented follow-up to the end of their treatment and/or monitoring or until August 31, 2011, were retrospectively monitored; the diagnosis and subsequent decision to treat was made by the patient's own physician. Assessments included the change in visual acuity (standardized letter count) during the first and second years after start of ranibizumab therapy and resource utilization.

RESULTS: Four hundred and ten patients from 13 UK centers were analyzed. The mean (standard deviation [SD]) letter score at baseline was 55.0 (17.8). The mean (SD) change in visual acuity from baseline was +6.0 (15.4) letters at year 1 and +4.1 (16.9) at year 2. Most of the patients (86.6%) completed a 3-month loading phase; the visual improvements were numerically higher in these patients. Over 2 years, the mean (SD) number of clinic visits and injections was 18.4 (5.0) and 9.0 (4.7), respectively. Resource use and visual acuity gains were greater than those observed in the global population, which included other countries enrolled in AURA (Canada, France, Germany, Ireland, Italy, the Netherlands, and Venezuela). When patients were stratified according to severity of nAMD (based on letter count at baseline), the mean change in visual acuity score at years 1 and 2 was also higher for the UK than for the global population across all subgroups.

CONCLUSION: Monitoring and treatment rates were high in the UK, resulting in better visual acuity outcomes compared with other included countries. This suggests that translation of clinical study outcomes into real-life settings is achievable, but at the expense of higher resource utilization than is currently the norm in most developed countries.

PMID: 26834453 [PubMed] PMCID: PMC4716754

Mol Pharm. 2016 Feb 2. [Epub ahead of print]

Economic and Quality of Life Benefits of Anti-VEGF Therapy.

Hodgson N, Wu F, Ferreyra H, Zhu J, Wang W, Zhang K, Wang J.

Abstract: Vision impairment and blindness create a significant impact on quality of life and loss of productivity. Health care expenditures for vision problems, including direct medical costs and indirect costs for support services and loss of productivity, amount to \$139 billion annually. It is projected that by 2020, 5 million people will have visual impairment due to age related macular degeneration and diabetic macular edema. VEGF inhibitor therapy has been shown to be a cost-effective treatment for age related macular degeneration and diabetic macular edema that has reduced the incidence of vision loss and can reduce the associated economic and societal cost.

PMID: 26836112 [PubMed - as supplied by publisher]

Mar Drugs. 2016 Feb 3;14(2).

Fucoidan as a Potential Therapeutic for Major Blinding Diseases-A Hypothesis.

Klettner A.

Abstract: Fucoidan is a heterogeneous group of sulfated polysaccharide with a high content of L-fucose, which can be extracted from brown algae and marine invertebrates. It has many beneficial biological activities that make fucoidan an interesting candidate for therapeutic application in a variety of diseases. Age-related macular degeneration and diabetic retinopathy are major causes for vision loss and blindness in the industrialized countries and increasingly in the developing world. Some of the characteristics found in certain fucoidans, such as its anti-oxidant activity, complement inhibition or interaction with the Vascular Endothelial Growth factor, which would be of high interest for a potential application of fucoidan in age-related macular degeneration or diabetic retinopathy. However, the possible usage of fucoidan in ophthalmological diseases has received little attention so far. In this review, biological activities of fucoidan that could be of interest regarding these diseases will be discussed.

PMID: 26848666 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Am J Ophthalmol. 2016 Feb 3. [Epub ahead of print]

Choroidal neovascularization analyzed on ultra-high speed swept source optical coherence tomography angiography compared to spectral domain optical coherence tomography angiography.

Novais EA, Adhi M, Moulton EM, et al

PURPOSE: To compare visualization of choroidal neovascularization (CNV) secondary to age-related macular degeneration (AMD) using an ultra-high speed swept-source (SS)-optical coherence tomography angiography (OCTA) prototype versus a spectral-domain (SD)-OCTA device.

DESIGN: Comparative analysis of diagnostic instruments.

METHODS: Patients were prospectively recruited to be imaged on SD-OCT and SS-OCT devices on the same day. The SD-OCT device employed is the RTVue Avanti that operates at ~840nm wavelength and 70,000 A-scans/second. The SS-OCT device used is an ultra-high speed long-wavelength prototype that operates at ~1050nm wavelength and 400,000 A-scans/second. Two observers independently measured the CNV area on OCTA en face images from the two devices using ImageJ. The non-parametric Wilcoxon signed-rank test was used to compare area measurements and p-values of <0.05 were considered statistically significant.

RESULTS: Fourteen eyes from 13 patients were enrolled. The CNV in 11 eyes (78.6%) were classified as type-1, 2 eyes (14.3%) as type-2, and 1 eye (7.1%) as mixed type. Total CNV area measured using SS-OCT and SD-OCT 3mm x 3mm OCTA were $0.949 \pm 1.168\text{mm}^2$ and $0.340 \pm 0.301\text{mm}^2$, respectively ($p=0.001$). For the 6mm x 6mm OCTA the total CNV area using SS-OCT and SD-OCT were $1.218 \pm 1.284\text{mm}^2$ and $0.604 \pm 0.597\text{mm}^2$, respectively ($p=0.0019$). The field of view did not significantly affect the measured CNV area ($p=0.19$ and $p=0.18$ for SS-OCT and SD-OCT respectively).

CONCLUSION: SS-OCTA yielded significantly larger CNV areas than SD-OCTA. It is possible that SS-OCTA is better able to demarcate the full extent of CNV vasculature.

PMID: 26851725 [PubMed - as supplied by publisher]

Arq Bras Oftalmol. 2016 Feb;79(1):4-8.

A study of the vitreoretinal interface in patients with age-related macular degeneration.

Martins Mde F, Volpatto E, Emery P, Serracarbassa PD.

PURPOSE: To assess whether hyaloid adhesion is more prevalent in patients with age-related macular

degeneration (AMD) than in control patients and to evaluate whether it is more prevalent in exudative AMD than in non-exudative AMD.

METHODS: This was a cross-sectional, controlled analytical study. Patients from the Ophthalmology Department of the Public Service Hospital of the State of São Paulo were included if they were diagnosed with AMD that was confirmed by fundus biomicroscopy and fluorescein angiography. Patients were divided into three groups: patients without a vitreoretinal disease (controls), patients with exudative AMD, and patients with non-exudative AMD. For the optimal study of the vitreoretinal interface, all patients were subjected to spectral-domain optical coherence tomography (SD-OCT; Cirrus HD-OCT, version 4000; Carl Zeiss Meditec) and ultrasonography (UltraScan®, Alcon). Results with p values of ≤ 0.05 were considered statistically significant.

RESULTS: We assessed 75 eyes of 23 patients with AMD (14 women and nine men) and 15 the control patients (11 women and four men). In total, 33 eyes had AMD that was consistent with the inclusion criteria, of which 11 had the non-exudative form (non-atrophic) and 22 had the exudative form (11 active and 11 disciform scars). Adherence was observed in eight eyes in the control group (26.67%), in seven eyes with exudative AMD (31.82%), and in five eyes with non-exudative AMD (45.45%).

CONCLUSION: Patients with exudative and non-exudative forms of AMD did not present with higher vitreoretinal adhesion than control patients as assessed by SD-OCT and ultrasound. Moreover, patients with exudative AMD (neovascular membrane and disciform scar) did not reveal a higher adherence than those with non-exudative AMD when evaluated by the same methods.

PMID: 26840157 [PubMed - in process]

Eur J Ophthalmol. 2016 Jan 22:0. [Epub ahead of print]

Patient perceptions and experiences of stereotactic radiotherapy for wet age-related macular degeneration.

Senra H, Joseph S, Balaskas K, Horani M, Aslam T.

PURPOSE: Wet age-related macular degeneration (ARMD) is a leading cause of visual impairment. Anti-vascular endothelial growth factor (VEGF) injections are the mainstay of treatment but require monthly injections and frequent hospital visits. A novel approach to treatment with the use of stereotactic radiotherapy (Oraya IRay) as an adjunct to ranibizumab injections has shown promising results. We explored patients' experiences of receiving Oraya therapy for wet ARMD.

METHODS: We present a consecutive case series with objective and detailed reporting of the personal experiences of 5 patients with active wet ARMD treated with Oraya radiotherapy in our unit. We provided all patients who had received one Oraya treatment with a standardized survey composed of 10 questions addressing the experience of receiving this treatment.

RESULTS: Generally, patients reported positive experiences of receiving Oraya treatment and perceived this treatment as a better option in comparison with anti-VEGF injections. However, the patients' perceptions of Oraya treatment varied according to patients' previous experiences of anti-VEGF injections and expectations of treatment.

CONCLUSIONS: Patients mainly justified their decision to receive Oraya treatment by expecting fewer intravitreal injections, but more research on this topic is needed to suggest new evidence-based treatment protocols for patients with wet ARMD.

PMID: 26833232 [PubMed - as supplied by publisher]

J Vis. 2016 Feb 1;16(3):1.

Smooth pursuit eye movements in patients with macular degeneration.

Shanidze N, Fusco G, Potapchuk E, Heinen S, Verghese P.

Abstract: Currently, there are no quantitative studies of smooth pursuit, a behavior attributed to the fovea, in individuals with macular degeneration (MD). We hypothesize that pursuit in MD patients depends on the relative positions of the scotoma and target trajectory. We tested this hypothesis with a scanning laser ophthalmoscope (SLO), which allows for direct visualization of the target on the damaged retina. Monocular microperimetry and eye movements were assessed in eleven individuals with differing degrees of MD. Observers were asked to visually track a 1.7° target that moved in one of eight radial directions at 5°/s-6°/s. Consistent with our hypothesis, pursuit metrics depended on whether the target moved into or out of scotoma. Pursuit gains decreased with increasing scotoma extent in the target's heading direction ($p = 0.017$). Latencies were higher when the scotoma was present along the target trajectory (in either starting or heading directions, $p < 0.001$). Furthermore, an analysis of retinal position shows that targets fell on the fixational locus nearly 50% of the time. The results suggest that MD patients are capable of smooth pursuit eye movements, but are limited by target trajectory and scotoma characteristics.

PMID: 26830707 [PubMed - in process]

J Diabetes Sci Technol. 2016 Feb 1. [Epub ahead of print]

The Evolution of Teleophthalmology Programs in the United Kingdom: Beyond Diabetic Retinopathy Screening.

Sim DA, Mitry D, Alexander P, Mapani A, Goverdhan S, Aslam T, Tufail A, Egan CA, Keane PA.

Abstract: Modern ophthalmic practice in the United Kingdom is faced by the challenges of an aging population, increasing prevalence of systemic pathologies with ophthalmic manifestations, and emergent treatments that are revolutionary but dependent on timely monitoring and diagnosis. This represents a huge strain not only on diagnostic services but also outpatient management and surveillance capacity. There is an urgent need for newer means of managing this surge in demand and the socioeconomic burden it places on the health care system. Concurrently, there have been exponential increases in computing power, expansions in the strength and ubiquity of communications technologies, and developments in imaging capabilities. Advances in imaging have been not only in terms of resolution, but also in terms of anatomical coverage, allowing new inferences to be made. In spite of this, image analysis techniques are still currently superseded by expert ophthalmologist interpretation. Teleophthalmology is therefore currently perfectly placed to face this urgent and immediate challenge of provision of optimal and expert care to remote and multiple patients over widespread geographical areas. This article reviews teleophthalmology programs currently deployed in the United Kingdom, focusing on diabetic eye care but also discussing glaucoma, emergency eye care, and other retinal diseases. We examined current programs and levels of evidence for their utility, and explored the relationships between screening, teleophthalmology, disease detection, and monitoring before discussing aspects of health economics pertinent to diabetic eye care. The use of teleophthalmology presents an immense opportunity to manage the steadily increasing demand for eye care, but challenges remain in the delivery of practical, viable, and clinically proven solutions.

PMID: 26830492 [PubMed - as supplied by publisher]

Mol Pharm. 2016 Feb 1. [Epub ahead of print]

Composite Nanoformulation Therapeutics for Long Term Ocular Delivery of Macromolecules.

Agrahari V, Agrahari V, Hung WT, Christenson L, Mitra AK.

Abstract: The purpose of this investigation is to design and synthesize novel pentablock (PB) copolymer

(PB-1: PCL-PLA-PEG-PLA-PCL) based nanoformulations suspended in a thermosensitive gelling copolymer (PB-2: mPEG-PCL-PLA-PCL-PEGm) termed as composite nanoformulation. The composite nanoformulation was prepared to provide a sustained delivery of macromolecules over a longer duration with negligible burst release effect. The delivery system was designed to be utilized for the treatment of posterior segment ocular diseases such as age-related (wet) macular degeneration, diabetic retinopathy, and diabetic macular edema. The novel PB copolymers were characterized for their functional groups by FT-IR spectroscopy, molecular weight and purity by ¹H-NMR spectroscopy and gel permeation chromatography. X-Ray diffraction analysis was used to determine the crystallinity of copolymers. The size distribution of PB-1 nanoparticles (NPs) prepared using emulsification-solvent evaporation method was found to be ~150 nm analyzed by nanoparticle tracking analysis. The % encapsulation efficiency and % drug loading were found to be 66.64% ± 1.75 and 18.17% ± 0.39, respectively, (n = 3). Different weight percentages (15wt% and 20wt%) of the PB-2 copolymer has been utilized for in vitro release studies of IgG-Fab from composite nanoformulation. A negligible burst release with continuous near zero-order release has been observed from the composite nanoformulation analyzed up to 80 days. In vitro cell viability and biocompatibility studies performed on ocular (human corneal epithelial and retinal pigment epithelium) and macrophage (RAW 264.7) cell lines, showed that the synthesized PB copolymer based composite nanoformulations were safe for clinical applications. Based on the results observed, it is concluded that PB copolymer based composite nanoformulations can serve as a platform for ocular delivery of therapeutic proteins. In addition, the composite nanoformulation may provide minimal side effects associated with frequent intravitreal injections.

PMID: 26828415 [PubMed - as supplied by publisher]

Cir Cir. 2016 Jan 27. [Epub ahead of print]

[Atypical presentation of central serous choroidopathy. Case report]. [Article in Spanish]

Hernández-Da Mota SE.

BACKGROUND: Central serous choroidopathy is a macular disease, usually with a self-limited and benign course, and predominantly affects male patients between 20 and 45 years old.

CLINICAL CASE: A 68 year-old female patient complained of decreased visual acuity of her right eye of approximately 3 weeks of onset. Best corrected visual acuity in her right eye was 20/100. Fundus examination revealed a macular serous detachment involving its centre, as well as the presence of multiple calcified drusen. Fluorescein angiography showed late parafoveal leakage in a "smokestack" pattern in the right macular area. Optical coherence tomography showed a dome-shape macular detachment, also in the right eye. The patient was observed every 2 weeks and spontaneous resolution of the macular detachment was seen a month later. Based on these clinical features, a diagnosis was made of central serous choroidopathy of atypical presentation.

CONCLUSIONS: Atypical presentation cases of serous central choroidopathy might be seen occasionally. Hence, it is an important differential diagnosis of age related macular degeneration in patients older than 60 years.

PMID: 26826892 [PubMed - as supplied by publisher]

J Fr Ophtalmol. 2016 Jan 27. [Epub ahead of print]

[Non-traumatic vitreous hemorrhage]. [Article in French]

Conart JB, Berrod JP.

Abstract: Spontaneous vitreous hemorrhage is a serious disease whose incidence is 7 per 100,000 people per year. Posterior vitreous detachment with or without retinal tear, diabetic retinopathy, vascular

proliferation after retinal vein occlusion, age-related macular degeneration and Terson's syndrome are the most common causes. Repeated ultrasonography may ignore a retinal tear or detachment and delay vitrectomy that is the only treatment for serious forms. The occurrence of retinal tear or detachment is a surgical emergency as well as rubeosis or diabetic tractional retinal detachment involving the macula. Intravitreal injection of antiangiogenic agents are helpful in clearing the vitreous cavity, facilitating laser photocoagulation and reducing the risks of bleeding during preretinal neovascular membranes dissection.

PMID: 26826742 [PubMed - as supplied by publisher]

Vestn Oftalmol. 2015 Sep-Oct;131(5):4-12.

[Optical coherence tomography angiography in the diagnosis of neovascular age-related macular degeneration]. [Article in Russian]

Shaimov TB, Panova IE, Shaimov RB, Shaimova VA, Shaimova TA, Fomin AV.

AIM: to determine optical coherence tomography (OCT) angiography signs of classic and occult choroidal neovascularization (CNV) in patients with age-related macular degeneration (AMD) and evaluate their information value in monitoring the effect of anti-VEGF therapy.

MATERIAL AND METHODS: The study enrolled 76 patients (87 eyes), including 68 patients (72 eyes) with wet AMD and 8 patients (15 eyes) with no signs of neovascularization. All patients underwent spectral-domain OCT, OCT angiography, and fluorescein angiography (FA). OCT angiography was used to evaluate neovascular networks in terms of their location, shape, size, and extent of visualization. Sensitivity and specificity of the method were assessed separately in a group of 37 CNV eyes and 15 unsuspecting eyes, specific findings at FA being the main diagnostic criteria. To determine the information value of OCT angiography in monitoring the effect of intravitreal ranibizumab therapy, 9 patients (9 eyes) were selected, in whom the exam was performed the day before the injection and then at days 3, 10, 17, 24, and 31.

RESULTS: The patients were divided into two groups. Group 1 consisted of 43 eyes with occult CNV, group 2--of 29 eyes with classic CNV. Neovascular loops underneath the retinal pigment epithelium were found in 76.74% of occult CNV cases. In patients with classic CNV, the neovascularity was clearly visible in 82.76% of eyes, loop-like and tree-like networks occurring with similar frequency (51.72% and 42.28% respectively). OCT angiography results obtained prior to and following ranibizumab injection revealed a change in not only the size of neovascularization, but also the density, thickness, and branching pattern of newly formed blood vessels. Sensitivity and specificity of OCT angiography has been shown to be 89.2% and 93.3% respectively.

CONCLUSION: OCT angiography enables diagnosis of both classic and occult choroidal neovascularization in patients with AMD as well as dynamic assessment of the size of the neovascular complex during anti-VEGF treatment. The method has high sensitivity and specificity.

PMID: 26845866 [PubMed - in process]

J Exp Neurosci. 2016 Feb 1;10:1-19. eCollection 2016.

Neuroprotective Effects Against POCD by Photobiomodulation: Evidence from Assembly/Disassembly of the Cytoskeleton.

Liebert AD, Chow RT, Bicknell BT, Varigos E.

Abstract: Postoperative cognitive dysfunction (POCD) is a decline in memory following anaesthesia and surgery in elderly patients. While often reversible, it consumes medical resources, compromises patient well-being, and possibly accelerates progression into Alzheimer's disease. Anesthetics have been implicated in POCD, as has neuroinflammation, as indicated by cytokine inflammatory markers. Photobiomodulation (PBM) is an effective treatment for a number of conditions, including inflammation.

PBM also has a direct effect on microtubule disassembly in neurons with the formation of small, reversible varicosities, which cause neural blockade and alleviation of pain symptoms. This mimics endogenously formed varicosities that are neuroprotective against damage, toxins, and the formation of larger, destructive varicosities and focal swellings. It is proposed that PBM may be effective as a preconditioning treatment against POCD; similar to the PBM treatment, protective and abscopal effects that have been demonstrated in experimental models of macular degeneration, neurological, and cardiac conditions.

PMID: 26848276 [PubMed]

Zhonghua Yan Ke Za Zhi. 2015 Nov;51(11):804-807.

[Clarifying some concepts and clinical significance of refractory or recurrent neovascular age-related macular degeneration]. [Article in Chinese]

Zhao J, Sun X.

Abstract: Anti-VEGF therapy is currently one of the main treatments for neovascular age-related macular degeneration (nAMD). Clinically, patients under standardized anti-VEGF therapy showed different responses, of which recurrences or even insensitivity were found in some patients. However, the specific definitions of these various clinical responses are still unclarified. Therefore, to consolidate and define these concepts are of great importance regarding to future efficacy comparison, treatment response clarification and novel drug switching therapies.

PMID: 26850580 [PubMed - as supplied by publisher]

Pan Afr Med J. 2015 Sep 22;22:61. eCollection 2015.

[Diagnostic approach of macular degeneration with "spectral-domain" OCT: clinical case]. [Article in French]

El Ouafi A, El Mellaoui M, Laktaoui A.

PMID: 26834914 [PubMed - in process] PMCID: PMC4725667 Free PMC Article

Pathogenesis

PLoS One. 2016 Feb 4;11(2):e0147684. eCollection 2016.

Evidence of Alternative Cystatin C Signal Sequence Cleavage Which Is Influenced by the A25T Polymorphism.

Nguyen A, Hulleman JD.

Abstract: Cystatin C (Cys C) is a small, potent, cysteine protease inhibitor. An Ala25Thr (A25T) polymorphism in Cys C has been associated with both macular degeneration and late-onset Alzheimer's disease. Previously, studies have suggested that this polymorphism may compromise the secretion of Cys C. Interestingly, we found that untagged A25T, A25T tagged C-terminally with FLAG, or A25T FLAG followed by green fluorescent protein (GFP), were all secreted as efficiently from immortalized human cells as their wild-type (WT) counterparts (e.g., 112%, 100%, and 88% of WT levels from HEK-293T cells, respectively). Supporting these observations, WT and A25T Cys C variants also showed similar intracellular steady state levels. Furthermore, A25T Cys C did not activate the unfolded protein response and followed the same canonical endoplasmic reticulum (ER)-Golgi trafficking pathway as WT Cys C. WT Cys C has been shown to undergo signal sequence cleavage between residues Gly26 and Ser27. While the A25T polymorphism did not affect Cys C secretion, we hypothesized that it may alter where the Cys C signal

sequence is preferentially cleaved. Under normal conditions, WT and A25T Cys C have the same signal sequence cleavage site after Gly26 (referred to as 'site 2' cleavage). However, in particular circumstances when the residues around site 2 are modified (such as by the presence of an N-terminal FLAG tag immediately after Gly26, or by a Gly26Lys (G26K) mutation), A25T has a significantly higher likelihood than WT Cys C of alternative signal sequence cleavage after Ala20 ('site 1') or even earlier in the Cys C sequence. Overall, our results indicate that the A25T polymorphism does not cause a significant reduction in Cys C secretion, but instead predisposes the protein to be cleaved at an alternative signal sequence cleavage site if site 2 is hindered. Additional N-terminal amino acids resulting from alternative signal sequence cleavage may, in turn, affect the protease inhibition function of Cys C.

PMID: 26845025 [PubMed - in process]

CNS Neurol Disord Drug Targets. 2016 Feb 2. [Epub ahead of print]

Inflammatory Mechanisms and Oxidative Stress as Key Factors Responsible for Progression of Neurodegeneration: Role of Brain Innate Immune System.

Leszek J, Barreto GE, Gąsiorowski K, Koutsouraki E, Ávila-Rodrigues M, Aliev G.

Abstract: Chronic inflammation is characterized by longstanding microglial activation followed by sustained release of inflammatory mediators, which aids in enhanced nitrosative and oxidative stress. The sustained release of inflammatory mediators propels the inflammatory cycle by increased microglial activation, promoting their proliferation and thus stimulating enhanced release of inflammatory factors. Elevated levels of several cytokines and chronic neuroinflammation has been associated with many neurodegenerative disorders of central nervous system like age-related macular degeneration, Alzheimer disease, multiple sclerosis, Parkinson's disease, Huntington' disease, and tauopathies. This review highlights the basic mechanisms of neuroinflammation, the characteristics of neurodegenerative diseases, and the main immunologic responses in CNS neurodegenerative disorders. A comprehensive outline for the crucial role of microglia in neuroinflammation and neurodegeneration and the role of Toll-like receptor signalling in coexistence of inflammatory mechanisms and oxidative stress as major factors responsible for progression of neurodegeneration have also been presented.

PMID: 26831258 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2016 Feb 1;57(2):312-9.

Interleukin-17A Induces IL-1 β Secretion From RPE Cells Via the NLRP3 Inflammasome.

Zhang S, Yu N, Zhang R, Zhang S, Wu J.

PURPOSE: Inflammasome activation and IL-1 β production have been proposed to have an important role in age-related macular degeneration (AMD). Growing evidence is emerging for involvement of interleukin-17A (IL-17A) in AMD pathogenesis. We investigated the effects of IL-17A on the activation of inflammasome and production of IL-1 β in primary human RPE cells.

METHODS: Primary human RPE cells were isolated and cultured for the following experiments. Expression patterns of IL-17 receptor A (IL-17RA), IL-17 receptor C (IL-17RC), and ACT1 were analyzed by RT-PCR, flow cytometry, and immunofluorescence. IL-17A was added to the cell cultures, and cytokine expression, signaling pathways, and inflammasome machinery were investigated using real-time RT-PCR, ELISA, Western blot, flow cytometry, and small interfering RNA.

RESULTS: Retinal pigment epithelial cells constitutively expressed IL-17RA, IL-17RC, and ACT1. IL-17A upregulated the mRNA levels of pro-IL-1 β , IL-8, CCL2, and CCL20, as well as the protein level of IL-1 β . IL-17A induced the phosphorylation of Akt, Erk1/2, p38 MAPK, and NF- κ B p65 in RPE cells. Blocking NF- κ B attenuated IL-17A-induced expression of pro-IL-1 β mRNA. IL-17A enhanced pro-caspase-1 and NLRP3

mRNA expression. Inhibiting caspase-1 activity and silencing NLRP3 decreased IL-1 β secretion, confirming NLRP3 as the IL-17A-responsive inflammasome on the posttranscriptional level. The mechanism of IL-17A-triggered NLRP3 activation and subsequent IL-1 β secretion was found to involve the generation of reactive oxygen species.

CONCLUSIONS: Our results suggest that IL-17A triggers a key inflammatory mediator, IL-1 β , from RPE cells, via NLRP3 inflammasome activation, holding therapeutic potential for AMD.

PMID: 26830368 [PubMed - in process]

Eur J Pharmacol. 2016 Feb 1. [Epub ahead of print]

TGF- β 1 prevents rat retinal insult induced by amyloid- β (1-42) oligomers.

Fisichella V, Giurdanella G, Maria Platania CB, Romano GL, Leggio GM, Salomone S, Drago F, Caraci F, Bucolo C.

Abstract: To set up a retinal degenerative model in rat that mimics pathologic conditions such as age-related macular degeneration (AMD) using amyloid- β (A β) oligomers, and assess the effect of TGF- β 1. Sprague-Dawley male rats were used. Human A β 1-42 oligomers were intravitreally (ITV) injected (10 μ M) in the presence or in the absence of recombinant human TGF- β 1 (1 ng/ μ l ITV injected). After 48h, the animals were sacrificed and the eyes removed and dissected. The apoptotic markers Bax and Bcl-2 were assessed by western blot analysis in retina lysates. Gene-pathway network analysis was carried out in order to identify pathways involved in AMD. Treatment with A β oligomers induced a strong increase in Bax protein level (about 4-fold; $p < 0.01$) and a significant reduction in Bcl-2 protein level (about 2-fold; $p < 0.05$). Co-injection of TGF- β 1 triggered a significant reduction of Bax protein induced by A β oligomers. Bioinformatic analysis revealed that Bcl-2 and PI3K-Akt are the most connected nodes, for genes and pathways respectively, in the enriched gene-pathway network common to AMD and Alzheimer disease (AD). Overall, these data indicate that ITV injection of A β 1-42 oligomers in rat induces molecular changes associated with apoptosis in rat retina, highlighting a potential pathogenetic role of A β oligomers in AMD. Bioinformatics analysis confirms that apoptosis pathways can take part in AMD. Furthermore, these findings suggest that human recombinant TGF- β 1 can prevent retinal damage elicited by A β oligomers.

PMID: 26845696 [PubMed - as supplied by publisher]

Immunobiology. 2016 Jan 16. [Epub ahead of print]

Increased serum IgA concentration and plasmablast frequency in patients with age-related macular degeneration.

Yu H, Yuan L, Yang Y, Ma S, Peng L, Wang Y, Zhang C, Li T.

Abstract: Age-related macular degeneration (AMD) is the leading cause of blindness among senior citizens of developed countries, with currently unknown etiology. Despite the close associations between AMD development and inhibitory complement factor H mutations, the first step of complement activation, which is the antibody response in AMD patients, has not been studied. Here, we obtained blood and tear samples from AMD patients and Non-AMD controls. We found that compared to Non-AMD controls, AMD subjects had increased IgA titers in serum and tear, and had elevated levels of circulating antibody-secreting plasmablasts. The increase in antibody titer was limited to the IgA isotype, since no significant differences were observed in IgM and IgG isotypes between AMD patients and Non-AMD controls. Interestingly, this increased antibody response in AMD patients was correlated with disease severity, as late AMD patients had increased IgA titers in serum and tear, as well as elevated plasmablast frequency after staphylococcal enterotoxin B stimulation, compared to early AMD patients. Together, our results implicated a role of overreactive IgA responses in AMD pathogenesis.

PMID: 26827241 [PubMed - as supplied by publisher]

J Biol Chem. 2016 Feb 2. [Epub ahead of print]

Angiopoietin-like protein 2 is a multistep regulator of inflammatory neovascularization in a murine model of age-related macular degeneration.

Hirasawa M, Takubo K, Osada H, Miyake S, Toda E, Endo M, Umezawa K, Tsubota K, Oike Y, Ozawa Y.

Abstract: Choroidal neovascularization (CNV) is a pathogenic process of age-related macular degeneration (AMD), a vision-threatening disease. The retinal pigment epithelium (RPE) and macrophages both influence CNV development. However, the underlying mechanisms remain obscure. Here, we focus on angiopoietin-like protein 2 (Angptl2), a cytokine involved in age-related systemic diseases. Angptl2 was originally identified as an adipocytokine, and is also expressed in the eye. Using a laser-induced CNV model, we found that Angptl2 KO mice exhibited suppressed CNV development with reduced macrophage recruitment and inflammatory mediator induction. The mediators monocyte chemoattractant protein-1, interleukin-1 β (IL-1 β), IL-6, matrix metalloproteinase-9 (Mmp-9), and transforming growth factor- β 1 (Tgf- β 1) that were upregulated during CNV development were all suppressed in the RPE-choroid of CNV models generated in the Angptl2 KO mice. Bone marrow transplantation using wild-type and KO mice suggested that both bone marrow-derived and host-derived Angptl2 were responsible for macrophage recruitment and CNV development. Peritoneal macrophages derived from Angptl2 KO mice expressed lower levels of the inflammatory mediators. In the wild-type peritoneal macrophages and RAW264.7 cells, Angptl2 induced the mediators via integrins α 4 and β 2, followed by the downstream activation of nuclear factor- κ B (NF- κ B) and ERK. The activation of NF- κ B and ERK by Angptl2 also promoted macrophage migration. Therefore, Angptl2 from focal tissue might trigger macrophage recruitment, and that from recruited macrophages might promote expression of inflammatory mediators including Angptl2 in an autocrine and/or paracrine fashion to facilitate CNV development. Angptl2 might therefore represent a multistep regulator of CNV pathogenesis, and serve as a new therapeutic target for AMD.

PMID: 26839315 [PubMed - as supplied by publisher]

J Biol Chem. 2016 Feb 4. [Epub ahead of print]

Phenotype-Based Discovery of 2-[(E)-2-(Quinolin-2-yl)vinyl]phenol as a Novel Regulator of Ocular Angiogenesis.

Reynolds AL, Alvarez Y, Sasore T, et al

Abstract: Retinal angiogenesis is tightly regulated to meet oxygenation and nutritional requirements. In diseases such as proliferative diabetic retinopathy and neovascular age-related macular degeneration, uncontrolled angiogenesis can lead to blindness. Our goal is to better understand the molecular processes controlling retinal angiogenesis and discover novel drugs that inhibit retinal neovascularisation. Phenotype-based chemical screens were performed using the ChemBridge Diverset™ library and inhibition of hyaloid vessel angiogenesis in Tg(fli1:EGFP) zebrafish. 2-[(E)-2-(Quinolin-2-yl)vinyl]phenol (quininib) robustly inhibits developmental angiogenesis at 4-10 μ M in zebrafish and significantly inhibits angiogenic tubule formation in HMEC-1 cells, angiogenic sprouting in aortic ring explants and retinal revascularisation in OIR mice. Quininib is well tolerated in zebrafish, human cell lines and murine eyes. Profiling screens of 153 angiogenic and inflammatory targets revealed quininib does not directly target VEGF receptors but antagonises cysteinyl leukotriene receptor 1 and 2 (CysLT1-2) at micromolar IC₅₀ values. In summary, quininib is a novel anti-angiogenic small molecule CysLT receptor antagonist. Quininib inhibits angiogenesis in a range of cell and tissue systems, revealing novel physiological roles for CysLT signalling. Quininib has potential as a novel therapeutic to treat ocular neovascular pathologies and may complement current anti-VEGF biologicals.

PMID: 26846851 [PubMed - as supplied by publisher]

Sci Rep. 2016 Feb 5;6:20639.

Impairing autophagy in retinal pigment epithelium leads to inflammasome activation and enhanced macrophage-mediated angiogenesis.

Liu J, Copland DA, Theodoropoulou S, Chiu HA, Barba MD, Mak KW, Mack M, Nicholson LB, Dick AD.

Abstract: Age-related decreases in autophagy contribute to the progression of age-related macular degeneration (AMD). We have now studied the interaction between autophagy impaired in retinal pigment epithelium (RPE) and the responses of macrophages. We find that dying RPE cells can activate the macrophage inflammasome and promote angiogenesis. In vitro, inhibiting rotenone-induced autophagy in RPE cells elicits caspase-3 mediated cell death. Co-culture of damaged RPE with macrophages leads to the secretion of IL-1 β , IL-6 and nitrite oxide. Exogenous IL-6 protects the dysfunctional RPE but IL-1 β causes enhanced cell death. Furthermore, IL-1 β toxicity is more pronounced in dysfunctional RPE cells showing reduced IRAK3 gene expression. Co-culture of macrophages with damaged RPE also elicits elevated levels of pro-angiogenic proteins that promote ex vivo choroidal vessel sprouting. In vivo, impaired autophagy in the eye promotes photoreceptor and RPE degeneration and recruitment of inflammasome-activated macrophages. The degenerative tissue environment drives an enhanced pro-angiogenic response, demonstrated by increased size of laser-induced choroidal neovascularization (CNV) lesions. The contribution of macrophages was confirmed by depletion of CCR2(+) monocytes, which attenuates CNV in the presence of RPE degeneration. Our results suggest that the interplay between perturbed RPE homeostasis and activated macrophages influences key features of AMD development.

PMID: 26847702 [PubMed - in process]

Epidemiology

Arq Bras Oftalmol. 2016 Feb;79(1):24-9.

Sociodemographic status of severely disabled and visually impaired elderly people in Turkey.

Kıvanç SA, Akova-Budak B, Olcaysü OO, Çevik SG.

PURPOSE: To identify the prevalence of ophthalmologic diseases in elderly patients who had been classified as severely disabled and to identify the ophthalmologic conditions leading to visual impairment and blindness.

METHODS: The medical records of 2806 patients who had applied to the Health Board of the Erzurum Region Training and Research Hospital between January 2011 and December 2012 were reviewed. One hundred ninety-nine patients aged >64 years who were classified as severely disabled with disability rates of over 50%, and who were unable to care for themselves or to move and/or communicate without help were included in the study.

RESULTS: The most frequently seen disabilities were neurological (47.2%) and those resulting from eye diseases (17.1%). The most common ophthalmologic diseases were cataract, glaucoma, and age-related macular degeneration. The mean right and left eye visual acuities were 1.17 ± 1.10 logMAR and 1.13 ± 1.0 logMAR, respectively. Of the 60 patients with ophthalmologic diseases or conditions, 33 were blind (visual acuity worse than 20/400) and 10 were visually impaired (visual acuity worse than 20/70 but better than 20/400). Cataracts were the main cause of blindness. The mean age of the patients who were still being followed up at the time of application to the disability board was significantly lower than that of the others ($p = 0.015$). Seventy-nine percent of the blind patients were from rural areas, and 88% of these had no regular follow-up. Among the blind and visually impaired, significantly more patients from urban areas had social security insurance (SSI) than those from rural areas ($p = 0.043$). Nearly 64% of the blind patients were women. The follow-up rate was significantly lower in women ($p = 0.025$). According to multinomial logistic regression analysis, the visually impaired and blind patients were more likely to have lower follow-up rates than the other types of severely disabled patients (OR: 0.231, 95% CI: 0.077-0.688, $p = 0.009$).

CONCLUSIONS: Blindness gives rise to severe disability, and the most common ophthalmologic diseases that cause severe disabilities in elderly patients are cataract, glaucoma, and age-related macular degeneration. Sociodemographic factors that may affect the accessibility of visually impaired and blind people to health services include their place of residence and gender.

PMID: 26840162 [PubMed - in process]

Genetics

Arch Soc Esp Oftalmol. 2016 Feb 2. [Epub ahead of print]

The presence of CFH, HTRA1, ARMS2, VEGF-A and VEGF-R and the appearance of age-related macular degeneration sub-types. [Article in English, Spanish]

Cruz-González F, Cabrillo Estévez L, Cañete Campos C, Sánchez-Jara Sánchez A, Juan Marcos L, González-Sarmiento R.

OBJECTIVE: To demonstrate the genetic influence in the onset of the different age-related macular disease (AMD) subtypes by analysing the genotype distribution of CFH, ARMS2, HTRA1, VEGF-A and VEGF-R polymorphisms in patients with neovascular and atrophic AMD.

MATERIALS AND METHODS: The study was conducted on 101 consecutive patients with AMD diagnosis (74 exudative, 27 atrophic) following Wisconsin international classification criteria. The CFH rs1410996, ARMS2 rs10940923, VEGF-A rs833061, rs699947, and VEGF-R rs2071559 polymorphisms were analysed using real time PCR with taqman probes, and HTRA1 rs112000638 using restriction endonucleases digestion. A study was made of the genotype distribution of the different polymorphisms in our group of patients with neovascular AMD and those with the atrophic type, and a comparison was made of the results for each one of the genes studied.

RESULTS: No statistically significant differences ($P > .05$) were found in the genotype distribution of the different polymorphisms between patients with neovascular AMD and patients with atrophic AMD in our population, although the "risk" genotypes tended to appear more frequently in patients with neovascular AMD, despite the lack of statistical significance.

CONCLUSIONS: Allelic variants of CFH, ARMS2, HTRA1, VEGF-A or VEGF-R genes are not associated with the different AMD subtypes. This suggests that, although the polymorphisms seem to be associated with the disease susceptibility, they are not involved in the onset of the different clinical variants of AMD. Further studies in different populations, and with a larger cohort of patients, are needed to confirm these results.

PMID: 26850328 [PubMed - as supplied by publisher]

Nat Commun. 2016 Feb 2;7:10561.

Genetic variants near MLST8 and DHX57 affect the epigenetic age of the cerebellum.

Lu AT, Hannon E, Levine ME, Hao K, Crimmins EM, Lunnon K, Kozlenkov A, Mill J, Dracheva S, Horvath S.

Abstract: DNA methylation (DNAm) levels lend themselves for defining an epigenetic biomarker of aging known as the 'epigenetic clock'. Our genome-wide association study (GWAS) of cerebellar epigenetic age acceleration identifies five significant ($P < 5.0 \times 10^{-8}$) SNPs in two loci: 2p22.1 (inside gene DHX57) and 16p13.3 near gene MLST8 (a subunit of mTOR complex 1 and 2). We find that the SNP in 16p13.3 has a cis-acting effect on the expression levels of MLST8 ($P = 6.9 \times 10^{-18}$) in most brain regions. In cerebellar samples, the SNP in 2p22.1 has a cis-effect on DHX57 ($P = 4.4 \times 10^{-5}$). Gene sets found by our GWAS analysis of cerebellar age acceleration exhibit significant overlap with those of Alzheimer's disease ($P = 4.4 \times$

10(-15)), age-related macular degeneration ($P=6.4 \times 10(-6)$), and Parkinson's disease ($P=2.6 \times 10(-4)$). Overall, our results demonstrate the utility of a new paradigm for understanding aging and age-related diseases: it will be fruitful to use epigenetic tissue age as endophenotype in GWAS.

PMID: 26830004 [PubMed - in process]

Ophthalmic Genet. 2016 Feb 5:1-6. [Epub ahead of print]

Genetic variants in complement pathway and ARMS2/HTRA1 genes and risk of age-related macular degeneration in a homogeneous population from central Greece.

Tsiloulis AN, Zacharaki F, Kotoula MG, Chatzoulis DZ, Morrison MA, Mayne K, Dardiotis E, Stefanidis IL, Almpantidou P, DeAngelis MM, Tsironi EE.

PMID: 26848857 [PubMed - as supplied by publisher]

Diet, lifestyle and low vision

Sci Rep. 2016 Feb 5;6:20723.

Dietary n-3 Fatty Acid, α -Tocopherol, Zinc, vitamin D, vitamin C, and β -carotene are Associated with Age-Related Macular Degeneration in Japan.

Aoki A, Inoue M, Nguyen E, Obata R, Kadonosono K, Shinkai S, Hashimoto H, Sasaki S, Yanagi Y.

Abstract: This case-control study reports the association between nutrient intake and neovascular age-related macular degeneration (AMD) in Japan. The nutrient intake of 161 neovascular AMD cases from two university hospitals and 369 population-based control subjects from a cohort study was assessed using a brief-type self-administered questionnaire on diet history, which required respondent recall of the usual intake of 58 foods during the preceding month. Energy-adjusted nutrient intake values were compared between the groups. Logistic regression analysis was used to estimate odds ratios (ORs) and 95% CIs adjusted for smoking history, age, sex, chronic disease history, supplement use, and alcohol consumption. Logistic regression analysis demonstrated that low intakes of n-3 fatty acid, α -tocopherol, zinc, vitamin D, vitamin C, and β -carotene were associated with neovascular AMD (Trend $P < 0.0001$ for n-3 fatty acid, Trend $P < 0.0001$ for α -tocopherol, Trend $P < 0.0001$ for zinc, Trend $P = 0.002$ for vitamin D, Trend $P = 0.04$ for vitamin C, Trend $P = 0.0004$ for β -carotene). There was no association with retinol or cryptoxanthin intake and neovascular AMD ($P = 0.67, 0.06$).

PMID: 26846575 [PubMed - in process]

Br J Ophthalmol. 2016 Feb 4. [Epub ahead of print]

Visual acuity loss in patients with age-related macular degeneration measured using a novel high-pass letter chart.

Shah N, Dakin SC, Dobinson S, Tufail A, Egan CA, Anderson RS.

BACKGROUND/AIMS: Conventional Logarithm of the Minimum Angle of Resolution (logMAR) acuity is the current gold standard for assessing visual function in age-related macular degeneration (AMD). However, visual acuity (VA) often remains 'normal' when measured with these charts, even with advanced retinal changes. We wished to investigate how VA measurements with the Moorfields Acuity Chart (MAC), which employs high-pass filtered letters, compares to conventional letter charts in subjects with AMD.

METHODS: Monocular best-corrected VA measurements and test-retest variability (TRV) were compared for conventional and MAC charts in 38 normal observers (mean age 52.1 years) and 80 patients (mean age

80.6 years) with varying degrees of acuity loss owing to AMD. Methods of Bland-Altman and ordinary least-squares regression were employed for data analysis.

RESULTS: A proportional bias was confirmed between conventional and MAC measurements ($r^2=0.133$, $p=0.001$) such that MAC acuity was -0.45 logMAR 'worse' at the 0.00 logMAR acuity level, but only -0.26 logMAR 'worse' at the 1.00 logMAR level. The mean bias was much smaller in the normal subject group (-0.16 logMAR). Similar TRV (ranging from ± 0.09 to ± 0.12 logMAR) was found for both charts in both subject groups.

CONCLUSIONS: VA measurements with the MAC chart appear to be more sensitive to functional loss in AMD compared with conventional letter charts, with similar TRV. Simulations indicate this may be because the high-pass filtered letters are more vulnerable to undersampling as a result of retinal cell loss in the disease process.

PMID: 26846435 [PubMed - as supplied by publisher]

Vestn Oftalmol. 2015 Sep-Oct;131(5):104-8.

**[Current data on the role of anthocyanosides and flavonoids in the treatment of eye diseases].
[Article in Russian]**

Vorob'eva IV.

Abstract: Anthocyanins are known to have antioxidant, anti-inflammatory, neuroprotective, and anticarcinogenic activity as well as positive effect on the cardiovascular system. Because of bilberry anthocyanosides (*Vaccinium myrtillus* L.), Mirtilene forte promotes rhodopsin synthesis and regeneration, increases retinal sensitivity to changes in light intensity, improves visual acuity and dark adaptation as well as blood supply of the retina. Studies conducted in Russia are aimed at evaluating the use of Mirtilene forte in age-related macular degeneration, diabetic retinopathy, primary open-angle glaucoma, and other diseases. This article provides an analysis of foreign and Russian publications on the effects of anthocyanins and flavonoids in different diseases.

PMID: 26845880 [PubMed - in process]

Dev Psychol. 2016 Feb 4. [Epub ahead of print]

Developmental Regulation With Progressive Vision Loss: Use of Control Strategies and Affective Well-Being.

Schilling OK, Wahl HW, Boerner K, Horowitz A, Reinhardt JP, Cimarolli VR, Brennan-Ing M, Heckhausen J.

Abstract: The present study addresses older adults' developmental regulation when faced with progressive and irreversible vision loss. We used the motivational theory of life span development as a conceptual framework and examined changes in older adults' striving for control over everyday goal achievement, and their association with affective well-being, in a sample of 364 older adults diagnosed with age-related macular degeneration. Using longitudinal data from 5 occasions at 6-month intervals, we examined intraindividual change in control strategies, and how it was related to change in affective well-being, in terms of self-rated happiness and depressive symptoms. Mixed model analyses confirmed our hypotheses that (a) intraindividual change, particularly in selective primary control and in compensatory secondary control (CSC), predict change toward higher happiness ratings and lower depression; and (b) as functional abilities (instrumental activities of daily living) declined, CSC became increasingly predictive of better affective well-being. Overall, the findings suggest that CSC strategies are essential for maintaining affective well-being when physical functioning declines. Intensified selective primary control striving may be effective to achieve goals that have become difficult to reach but are not associated with affective well-being, possibly because struggling with difficulties undermines the experience of enjoyable mastery. In contrast,

goal adjustments and self-protective thinking may help to find pleasure even from restricted daily activities.
(PsycINFO Database Record

PMID: 26845507 [PubMed - as supplied by publisher]

JAMA. 2016 Feb 2;315(5):516-7.

Oral Nutrient Supplementation and Cognitive Function--Reply.

Chew EY, Launer L, Bernstein P.

Comment on: Oral Nutrient Supplementation and Cognitive Function. [JAMA. 2016]

Effect of Omega-3 Fatty Acids, Lutein/Zeaxanthin, or Other Nutrient Supplementation on Cognitive Function: The AREDS2 Randomized Clinical Trial. [JAMA. 2015]

Oral Nutrient Supplementation and Cognitive Function. [JAMA. 2016]

PMID: 26836739 [PubMed - indexed for MEDLINE]

JAMA. 2016 Feb 2;315(5):516.

Oral Nutrient Supplementation and Cognitive Function.

Yurko-Mauro K, Nelson E, Salem N Jr.

Comment in: Oral Nutrient Supplementation and Cognitive Function--Reply. [JAMA. 2016]

Comment on: Effect of Omega-3 Fatty Acids, Lutein/Zeaxanthin, or Other Nutrient Supplementation on Cognitive Function: The AREDS2 Randomized Clinical Trial. [JAMA. 2015]

PMID: 26836738 [PubMed - indexed for MEDLINE]

JAMA. 2016 Feb 2;315(5):515-6.

Oral Nutrient Supplementation and Cognitive Function.

Renzi-Hammond LM, Miller LS, Hammond BR Jr.

Comment in: Oral Nutrient Supplementation and Cognitive Function--Reply. [JAMA. 2016]

Comment on: Effect of Omega-3 Fatty Acids, Lutein/Zeaxanthin, or Other Nutrient Supplementation on Cognitive Function: The AREDS2 Randomized Clinical Trial. [JAMA. 2015]

PMID: 26836737 [PubMed - indexed for MEDLINE]

Diabetes Res Clin Pract. 2016 Jan 15. [Epub ahead of print]

Metabolic syndrome and eye diseases.

Poh S, Mohamed Abdul RB, Lamoureux EL, Wong TY, Sabanayagam C.

Abstract: Metabolic syndrome is becoming a worldwide medical and public health challenge as it has been seen increasing in prevalence over the years. Age-related eye diseases, the leading cause of blindness globally and visual impairment in developed countries, are also on the rise due to aging of the population. Many of the individual components of the metabolic syndrome have been shown to be associated with

these eye diseases. However, the association of metabolic syndrome with eye diseases is not clear. In this review, we reviewed the evidence for associations between metabolic syndrome and certain ocular diseases in populations. We also reviewed the association of individual metabolic syndrome components with ocular diseases due to a paucity of research in this area. Besides, we also summarised the current understanding of etiological mechanisms of how metabolic syndrome or the individual components lead to these ocular diseases. With increasing evidence of such associations, it may be important to identify patients who are at risk of developing metabolic syndrome as prompt treatment and intervention may potentially decrease the risk of developing certain ocular diseases.

PMID: 26838669 [PubMed - as supplied by publisher]

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