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MD Research News

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Drug treatment

Ophthalmology. 2015 Oct 30. [Epub ahead of print]

Intravitreal Aflibercept for Macular Edema Following Branch Retinal Vein Occlusion: 52-Week Results of the VIBRANT Study.

Clark WL, Boyer DS, Heier JS, Brown DM, Haller JA, Vitti R, Kazmi H, Berliner AJ, Erickson K, Chu KW, Soo Y, Cheng Y, Campochiaro PA.

PURPOSE: To determine week 52 efficacy and safety outcomes in eyes with macular edema after branch retinal vein occlusion (BRVO) treated with 2 mg intravitreal aflibercept injection (IAI) compared with grid laser.

DESIGN: VIBRANT was a double-masked, randomized, phase 3 trial.

PARTICIPANTS: Eyes randomized and treated in VIBRANT were followed to week 52.

METHODS: In the IAI group, eyes received IAI every 4 weeks through week 24 and IAI every 8 weeks through week 48 with rescue grid laser if needed at week 36. In the grid laser group, all eyes received grid laser at baseline and, if prespecified rescue criteria were met, 1 additional laser from week 12 to 20 and IAI every 8 weeks after 3 monthly doses from week 24 onward (the laser/IAI group).

MAIN OUTCOME MEASURES: The primary outcome measure was percentage of eyes with improvement from baseline best-corrected visual acuity (BCVA) letter score ≥15 at week 24. All outcome measures at week 52 were exploratory, and P values are considered nominal.

RESULTS: The percentage of eyes with improvement from baseline letter score ≥15 in the IAI and laser/IAI groups was 52.7% versus 26.7% (P = 0.0003) at week 24 and 57.1% versus 41.1% (P = 0.0296) at week 52. The corresponding mean change from baseline BCVA letter score was 17.0 versus 6.9 (P < 0.0001) at week 24 and 17.1 versus 12.2 (P = 0.0035) at week 52. The mean reduction from baseline central retinal thickness was 280.5 μm versus 128.0 μm (P < 0.0001) at week 24 and 283.9 μm versus 249.3 μm (P = 0.0218) at week 52. In the IAI group, 10.6% of eyes received rescue laser at week 36, and in the laser/IAI group, 80.7% received rescue IAI from week 24 to week 48. Traumatic cataract in 1 eye (1.1%) in the IAI group was the only ocular serious adverse event.

CONCLUSIONS: After 6 monthly IAI, injections every 8 weeks maintained control of macular edema and visual benefits through week 52. In the laser group, rescue IAI given from week 24 onward resulted in substantial visual improvements at week 52.

PMID: 26522708 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2015 Nov 5. [Epub ahead of print]

Predicting vision gains with anti-VEGF therapy in neovascular age-related macular degeneration patients by using low-luminance vision.

Frenkel RE, Shapiro H, Stoilov I.

BACKGROUND/AIMS: To evaluate baseline low-luminance visual acuity (LLVA) as a predictor of visual acuity improvement in patients with neovascular (wet) age-related macular degeneration (wAMD) receiving antivascular endothelial growth factor A (anti-VEGF) therapy.

METHODS: In the HARBOR trial, 1084 treatment-naïve patients ≥50 years of age with subfoveal wAMD received intravitreal ranibizumab 0.5 or 2.0 mg monthly or as needed. To measure LLVA, patients read a normally illuminated ETDRS (Early Treatment Diabetic Retinopathy Study) chart with a neutral density filter placed in front of the study eye. Patients were assigned into quartiles based on the magnitude of the difference between best-corrected visual acuity under optimal luminance (BCVA) and LLVA (BCVA-LLVA gap). The association between mean change in BCVA from baseline and BCVA-LLVA gap at baseline was analysed using a general linear model.

RESULTS: A smaller baseline BCVA-LLVA gap predicted significantly higher BCVA gains over 24 months ($p<0.0001$ at each month; Pearson correlation), even after controlling for baseline BCVA or stratifying by treatment arm. Patients in the smallest baseline BCVA-LLVA gap quartile gained an average of +13.4 letters compared with +2.4 letters for patients in the widest baseline BCVA-LLVA gap quartile. At months 12 and 24, the smallest baseline BCVA-LLVA gap quartile had the highest proportion of ≥15-≥30-letter gain, and the widest baseline BCVA-LLVA gap quartile had the highest proportion of ≥15-/≥30-letter loss ($p<0.0001$; Fisher's exact test).

CONCLUSIONS: The baseline BCVA-LLVA gap is a significant predictor of visual acuity response to anti-VEGF treatment in patients with wAMD.

PMID: 26541435 [PubMed - as supplied by publisher] Free full text

JAMA Ophthalmol. 2015 Nov 5:1-4. [Epub ahead of print]

Effect of Regulatory Requirement for Patient-Specific Prescriptions for Off-Label Medications on the Use of Intravitreal Bevacizumab.

Holfinger S, Miller AG, Rao LJ, Rowland DY, Hornik JH, Miller DG.

IMPORTANCE: Requirements regulating pharmaceutical prescriptions can affect physicians' choice of therapy in a clinical setting.

OBJECTIVE: To evaluate the change in bevacizumab use after the regulatory requirement for patient-specific prescriptions (PSPs) for off-label medications in Ohio.

DESIGN, SETTING, AND PARTICIPANTS: This study retrospectively reviewed the aggregate data from the billing records of patients receiving 1.25-mg injections of bevacizumab, 0.3- or 0.5-mg injections of ranibizumab, or 2.0-mg injections of aflibercept for age-related macular degeneration or diabetic macular edema in a 9-member retinal specialty private practice. The review assessed 4488 intravitreal injections in the 3-month period before (May 1 to July 30, 2012) and 5253 injections in the 3-month period after (May 1 to July 30, 2013) the Ohio Board of Pharmacy's requirement of PSPs for bevacizumab. Relative proportions of the drugs used for intravitreal injections were calculated and frequencies were compared. A Likert scale survey was conducted among the 9 physicians to identify reasons for their change in prescription of bevacizumab. The survey inquired about (1) the burden of PSPs, (2) concern about differences in efficacy, and (3) concern about differences in safety.

MAIN OUTCOMES AND MEASURES: Difference in drug use before and after the PSP requirement for

bevacizumab and the physicians' reasons for change in their drug use.

RESULTS: Bevacizumab use decreased from 2752 of 4488 pre-PSP injections (61.3%) to 1503 of 5253 post-PSP injections (28.6%), a change of -32.7% (95% CI, -34.6% to -30.8%; P < .001). Use of 0.5-mg ranibizumab injections increased from 1122 of 4488 pre-PSP injections (25.0%) to 1838 of 5253 post-PSP injections (35.0%), a change of 10.0% (95% CI, 8.2% to 11.8%; P < .001). Use of 0.3-mg ranibizumab injections increased from 0 of 4488 (before US Food and Drug Administration approval) to 429 of 5253 post -PSP injections (8.2%), a change of 8.2% (95% CI, 7.4% to 8.9%; P < .001). Use of aflibercept injections increased from 614 of 4488 pre-PSP injections (13.7%) to 1483 of 5253 post-PSP injections (28.2%), a change of 14.6% (95% CI, 13.0%-16.1%; P < .001). In the survey of the 9 physicians concerning their reasons for decreased use of bevacizumab, 7 (78%) strongly agreed and 1 (11%) agreed that the burden of PSPs changed their choice of drug used for injection.

CONCLUSIONS AND RELEVANCE: Use of bevacizumab was reduced by 32.7% 1 year after the regulatory requirement for PSPs for compounded (repackaged) medications. This change seemed to have more association with the requirement for PSPs than with a known change in efficacy or safety concerns. Although this study was based on a single US practice, regulation of repackaged medication for safety concerns should also consider the evaluation of treatment burden, cost, and adherence.

PMID: 26540671 [PubMed - as supplied by publisher]

Retina. 2015 Nov 2. [Epub ahead of print]

INTRAVITREAL BEVACIZUMAB FOR CHOROIDAL NEOVASCULARIZATION IN AGE-RELATED MACULAR DEGENERATION: 5-Year Results of The Pan-American Collaborative Retina Study Group.

Arevalo JF, Lasave AF, Wu L, Acón D, Berrocal MH, Diaz-Llopis M, Gallego-Pinazo R, Serrano MA, Alezzandrini AA, Rojas S, Maia M, Lujan S; Pan-American Collaborative Retina Study Group (PACORES).

PURPOSE: To report the long-term anatomical and functional outcomes of patients with choroidal neovascularization secondary to age-related macular degeneration treated with intravitreal bevacizumab (IVB).

METHODS: Retrospective case series. Patients diagnosed with subfoveal choroidal neovascularization secondary to age-related macular degeneration that were treated with at least 1 intravitreal injection of 1.25 mg of IVB and had a minimum follow-up of 60 months. Patients underwent best-corrected Snellen visual acuity testing, optical coherence tomography, and ophthalmoscopic examination at baseline and follow-up visits.

RESULTS: Two hundred and forty-seven consecutive patients (292 eyes) were included. The mean number of IVB injections per eye was 10.9 ± 6.4. At 5 years, the BCVA decreased from 20/150 (logMAR 0.9 ± 0.6) at baseline to 20/250 (logMAR 1.1 ± 0.7) (P = <0.0001). The mean CMT decreased from 343.1+ 122.3 μm at baseline to 314.7 ± 128.8 μm at 60 months of follow-up (P = 0.009). Geographic atrophy (GA) was observed at baseline in 47 (16%) of 292 eyes. By 5 years, GA developed or progressed in 124 (42.5%) of 292 eyes (P < 0.0001).

CONCLUSION: The early visual gains obtained from IVB were not maintained at 5 years of follow-up. In addition, IVB may play a role in the development or progression of GA.

PMID: 26529555 [PubMed - as supplied by publisher]

J Fr Ophtalmol. 2015 Oct 28. [Epub ahead of print]

[Treatment of postoperative cystoid macular edema (Irvine-Gass syndrome) with dexamethasone 0.7mg intravitreal implant]. [Article in French]

Landré C, Zourdani A, Gastaud P, Baillif S.

PURPOSE: To evaluate the efficacy of dexamethasone 0.7mg intravitreal implant in patients with postoperative cystoid macular edema.

MATERIALS AND METHODS: Fourteen patients' charts with postoperative cystoid macular edema were retrospectively reviewed. The main outcome measures were best-corrected visual acuity (BCVA) and mean central retinal thickness (CRT).

RESULTS: Patients' mean age was 72.1 years old. Five patients were diabetic. All patients had previously been treated with non-steroidal anti-inflammatory drops. Four patients had received a previous treatment with intravitreal ranibizumab. The mean follow-up period was 8.7 months. Mean BCVA before intravitreal dexamethasone was 0.72 logMAR. After injection, it improved to 0.50 at month 1, was 0.47 at month 3, and 0.60 logMAR at month 12. The pre-injection mean CRT was 598µm. It improved to 286µm at month 1, 338µm at month 3, and was 441µm at month 12. Eight patients received 2 intravitreal injections of dexamethasone. Five patients presented with elevated intraocular pressure during follow-up, which was treated with drops.

CONCLUSIONS: Intravitreal dexamethasone injection improved visual acuity and macular thickness at month 1 and month 3 in patients with postoperative cystoid macular edema. A second injection was necessary after a mean period of 5 months.

PMID: 26520410 [PubMed - as supplied by publisher]

Ophthalmology. 2015 Oct 28. [Epub ahead of print]

Effect of Vitreomacular Adhesion on Treatment Outcomes in the Ranibizumab for Edema of the Macula in Diabetes (READ-3) Study.

Sadiq MA, Soliman MK, Sarwar S, Agarwal A, Hanout M, Demirel S, Rentiya ZS, Khan W, Do DV, Nguyen QD, Sepah YJ; READ-3 Study Group.

PURPOSE: To assess the role of vitreomacular adhesion (VMA) in visual and anatomic outcomes in patients with diabetic macular edema (DME).

DESIGN: Retrospective cohort study.

PARTICIPANTS: Data from patients enrolled in the Ranibizumab for Edema of the Macula in Diabetes: Protocol 3 with High Dose (READ-3) study were analyzed.

METHODS: In the READ-3 study, patients with DME received monthly intravitreal injections of either 0.5 or 2.0 mg ranibizumab. Optical coherence tomography images from patients who completed the month 6 visit of the study were analyzed at the baseline visit to identify the presence (VMA+) or absence (VMA-) of VMA. Patients with any degree of vitreomacular traction were excluded from the analysis. Two independent graders graded all images. Vitreomacular adhesion was classified by size of adhesion into either focal (<1500 µm) or broad (≥1500 µm).

MAIN OUTCOME MEASURES: Mean changes in best-corrected visual acuity (BCVA) and central retinal thickness (CRT) at month 6 and incidence of posterior vitreous detachment (PVD).

RESULTS: One hundred fifty-two eyes (152 patients) were randomized in the READ-3 study. One hundred twenty-four eyes (124 patients) were eligible for the study based on study criteria. Twenty-eight eyes did not meet study criteria and were excluded from the study. At baseline, 26 patients were classified as VMA+ and 98 patients were classified as VMA-. The distribution of the 2 doses of ranibizumab (0.5 and 2.0 mg) in the 2 groups was similar. At month 6, the mean improvement in BCVA was 11.31±6.67 and 6.86±7.58 letters in the VMA+ and VMA- groups, respectively (P = 0.007). Mean improvement in CRT was -173.81±132.31 and -161.84±131.34 µm in the VMA+ and VMA- groups, respectively (P = 0.681). At month 6, among the 26 VMA+ eyes (at baseline), 7 eyes demonstrated PVD, 17 eyes showed no change in VMA

status, and 2 eyes were not gradable and were excluded.

CONCLUSIONS: Diabetic macular edema patients with VMA have a greater potential for improvement in visual outcomes with anti-vascular endothelial growth factor therapy. Therefore, the presence of VMA should not preclude patients with DME from receiving treatment.

PMID: 26520169 [PubMed - as supplied by publisher]

Ophthalmic Res. 2015 Nov 6;55(1):10-18. [Epub ahead of print]

Treatment of Retinal Vein Occlusion with Ranibizumab in Clinical Practice: Longer-Term Results and Predictive Factors of Functional Outcome.

Farinha C, Marques JP, Almeida E, Baltar A, Santos AR, Melo P, Costa M, Figueira J, Cachulo ML, Pires I, Silva R.

PURPOSE: To evaluate long-term results and predictors of efficacy in patients with macular edema due to retinal vein occlusion (RVO) treated with intravitreal ranibizumab in a clinical practice setting.

METHODS: The clinical records of patients with a minimum follow-up of 3 years were retrospectively analyzed. Sixteen eyes with branch RVO (BRVO) and 16 with central RVO (CRVO) were included. All patients performed cross-sectional evaluation with best-corrected visual acuity (BCVA), spectral domain optical coherence tomography and fluorescein angiography. The foveal avascular zone (FAZ) was assessed and microstructural morphology of the retina was characterized.

RESULTS: Follow- up was 42.9 ± 9.0 and 44.8 ± 8.0 months in the CRVO and BRVO groups, respectively. Patients with CRVO received on average 6.9 injections, with a final VA gain of 8.3 ± 15.0 letters ($p = 0.05$). BRVO eyes had on average 5.9 injections, with a final VA gain of 1.6 ± 21.0 letters ($p > 0.05$). The FAZ area remained stable in both groups ($p > 0.05$). Baseline BCVA and disruption of the retinal pigment epithelium (RPE) were predictors of final BCVA ($p = 0.001$ and 0.011, respectively).

CONCLUSION: Although functional outcomes were inferior to those reported in clinical trials, ranibizumab was satisfactory in the long-term treatment of macular edema secondary to RVO and was not associated with increased macular ischemia. Final BCVA depends on baseline BCVA and RPE integrity.

PMID: 26540281 [PubMed - as supplied by publisher]

Ophthalmologica. 2015 Nov 6. [Epub ahead of print]

Fluctuations in Pigment Epithelial Detachment and Retinal Fluid Using a Bimonthly Treatment Regimen with Aflibercept for Neovascular Age-Related Macular Degeneration.

Zinkernagel MS, Wolf S, Ebneter A.

PURPOSE: To assess the effect of a bimonthly treatment regimen with intravitreal aflibercept on retinal fluid and pigment epithelial detachment (PED) in patients with neovascular age-related macular degeneration (AMD).

METHODS: Twenty-six treatment-naive eyes of 26 patients with choroidal neovascularisation secondary to AMD were included. The patients received three initial monthly (mean 30 days) intravitreal injections of aflibercept followed by a bimonthly (mean 62 days) fixed regimen for a total of 1 year. Best-corrected visual acuity (BCVA) and optical coherence tomography (OCT) measurements were recorded at monthly intervals. In addition, the presence of intraretinal fluid (IRF) or subretinal fluid (SRF) or a combination of both as well as serous and fibrovascular PEDs were assessed.

RESULTS: The mean patient age was 80 years (range 54-93). There were 14 male and 12 female patients. The mean gain in BCVA at 1 year was 9.3 letters (SEM ±3) with a mean reduction of the central retinal

thickness of 154 µm (SEM ±50). After 3 monthly injections of aflibercept, there was resolution of IRF and SRF in 80% of the treated eyes; the amount of fluid increased at months 4, 6 and 8 with troughs in between. Whereas fibrovascular PEDs remained stable after the loading phase, serous PEDs displayed a seesaw pattern. Patients without retinal pigment epithelium (RPE) atrophy at the end of the 1-year period had significantly better BCVA compared to patients with RPE atrophy (p = 0.03).

CONCLUSION: Despite significant overall BCVA gain, bimonthly intervals seem insufficient to maintain the morphological improvements after the initial loading dose with intravitreal aflibercept.

PMID: 26540259 [PubMed - as supplied by publisher]

CPT Pharmacometrics Syst Pharmacol. 2015 Oct;4(10):595-604. Epub 2015 Oct 8.

Population Pharmacokinetics and Pharmacodynamics of Lampalizumab Administered Intravitreally to Patients With Geographic Atrophy.

Le KN, Gibiansky L, van Lookeren Campagne M, Good J, Davancaze T, Loyet KM, Morimoto A, Strauss EC, Jin JY.

Abstract: Intravitreally administered lampalizumab is an investigational complement inhibitor directed against complement factor D (CFD) for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration. We sought to develop an integrated ocular and systemic pharmacokinetic/pharmacodynamic model for lampalizumab in patients with GA using the data from the clinical phase I and II studies. The kinetics of lampalizumab and CFD disposition were well described by the combined ocular/serum target-mediated drug disposition model using a quasi-steady-state approximation. This model takes into account the drug, target, and drug-target complex clearance, their transfer rates between ocular and serum compartments, and turnover kinetics of CFD. The constructed model provided a prediction of target occupancy in ocular tissues and supported that the two dosing regimens (10 mg q4w and 10 mg q6w) selected for the phase III studies are expected to be efficacious and able to achieve near-complete target engagement in the vitreous humor.

PMID: 26535160 [PubMed] PMCID: PMC4625864

Acta Ophthalmol. 2015 Nov 2. [Epub ahead of print]

Needle size in intravitreal injections - pain evaluation of a randomized clinical trial.

Haas P, Falkner-Radler C, Wimpissinger B, Malina M, Binder S.

PURPOSE: To evaluate the influence of the needle size used for intravitreal (IVT) injections on patients' pain experience in a randomized, double-armed, single-blinded, clinical trial.

METHODS: Patients included were randomized to have an IVT injection performed with a 27-gauge needle (group 1) or with a 30-gauge needle (group 2). The topical anaesthesia before the injection was standardized. Immediately after the injection, patients were asked to grade their pain using the visual analogue scale (VAS) and the Wong-Baker FACES scale. The main outcome measure was the pain score assessment. Cofactors analysed were patients' demographics (age and gender) and clinical characteristics (such as the number of previous IVT injections). In addition, scaled surgeon's questionnaires to assess the IVT injection procedure were evaluated. For statistical analysis, a regression model was used.

RESULTS: The data of 208 patients (group 1: 104 patients; group 2: 104 patients) were analysed. There was no significant difference in the VAS pain scores (p > 0.18) and in the Wong-Baker pain scores (p > 0.59) between both treatment groups. Gender (p = 0.0288) and the number of previous IVT injections (p = 0.0028) significantly influenced the VAS pain scores (p < 0.05). Female patients and patients with a history of previous IVT injections had higher pain scores. The surgeon's questionnaire showed an overall

preference towards the use of a 30-gauge needle for IVT injections.

CONCLUSION: The use of a 30-gauge needle for IVT injections showed no significant effect in pain relief compared to the use of a 27-gauge needle. However, a 30-gauge needle was preferred by all surgeons.

PMID: 26521866 [PubMed - as supplied by publisher]

Value Health. 2015 Nov;18(7):A428-9. Epub 2015 Oct 20.

Treatment of Macular Edema: What's New? Evidence From An Hta Study Comparing Ranibizumab And Dexamethasone Implant.

Ferrario L, Foglia E, Bandello F, Ferri C, Figini I, Franzin M, Gambaro G, Introini U, Medaglia M, Staurenghi G, Tadini P, Croce D.

PMID: 26532411 [PubMed - in process]

Value Health. 2015 Nov;18(7):A423. Epub 2015 Oct 20.

Health And Economic Outcomes Related to Delay Between Medical Indication and Treatment With Ranibizumab In Age-Related Macular Degeneration In Greece.

Kourlaba G, Chatzikou M, Pantelopoulou G, Maniadakis N.

PMID: 26532385 [PubMed - in process]

Other treatment & diagnosis

Ophthalmology. 2015 Nov 3. [Epub ahead of print]

Association between Antiplatelet or Anticoagulant Drugs and Retinal or Subretinal Hemorrhage in the Comparison of Age-Related Macular Degeneration Treatments Trials.

Ying GS, Maguire MG, Daniel E, Grunwald JE, Ahmed O, Martin DF; Comparison of Age-Related Macular Degeneration Treatments Trials Research Group.

PURPOSE: To evaluate the association between use of antiplatelet or anticoagulant drugs and retinal or subretinal hemorrhage in participants with neovascular age-related macular degeneration (AMD) in the Comparison of AMD Treatments Trials (CATT).

DESIGN: Cohort study within CATT.

PARTICIPANTS: Participants in CATT with untreated active neovascular AMD (n = 1185).

METHODS: Participants were interviewed for use of antiplatelet or anticoagulant drugs. Trained readers evaluated photographs for the presence and size of retinal or subretinal hemorrhage at baseline and years 1 and 2. Associations between use of antiplatelet or anticoagulant drugs and hemorrhage were evaluated among all participants and by baseline hypertension status using multivariate logistic regression models.

MAIN OUTCOME MEASURES: Odds ratio for association with antiplatelet or anticoagulant use.

RESULTS: Among 1165 participants with gradable photographs, 724 (62.1%) had retinal or subretinal hemorrhage at baseline; 84.4% of hemorrhages were 1 disc area (DA) or less, 8.1% were 1 to 2 DA, and 7.5% were more than 2 DA. At baseline, 608 participants (52.2%) used antiplatelet or anticoagulant drugs,

including 514 participants (44.1%) using antiplatelets only, 77 (6.6%) using anticoagulants only, and 17 (1.5%) using both. Hemorrhage was present in 64.5% of antiplatelet or anticoagulant users and in 59.6% of nonusers (P = 0.09; adjusted odds ratio [OR], 1.18; 95% confidence interval, 0.91-1.51; P = 0.21). Neither presence nor size of baseline hemorrhage was associated with the type, dose, or duration of antiplatelet or anticoagulant use. Forty-four of 1078 participants (4.08%) had retinal or subretinal hemorrhage detected on 1- or 2-year photographs; these hemorrhages were not associated with antiplatelet or anticoagulant use at baseline (P = 0.28) or during follow-up (P = 0.64). Among participants with hypertension (n = 807), antiplatelet or anticoagulant use was associated with a higher rate of hemorrhage at baseline (66.8% vs. 56.4%; adjusted OR, 1.48; P = 0.01), but not size of retinal or subretinal hemorrhage (P = 0.41).

CONCLUSIONS: Most retinal or subretinal hemorrhages in eyes enrolled in CATT were less than 1 DA. Among all CATT participants, antiplatelet or anticoagulant use was not associated significantly with hemorrhage, but it was associated significantly with hemorrhage in participants with hypertension.

PMID: 26545320 [PubMed - as supplied by publisher]

Ophthalmology. 2015 Oct 30. [Epub ahead of print]

Delayed Rod-Mediated Dark Adaptation Is a Functional Biomarker for Incident Early Age-Related Macular Degeneration.

Owsley C, McGwin G Jr, Clark ME, Jackson GR, Callahan MA, Kline LB, Witherspoon CD, Curcio CA.

PURPOSE: To examine whether slowed rod-mediated dark adaptation (DA) in adults with normal macular health at baseline is associated with the incidence of age-related macular degeneration (AMD) 3 years later.

DESIGN: Prospective cohort.

PARTICIPANTS: Adults aged ≥60 years were recruited from primary care ophthalmology clinics. Both eyes were required to be step 1 (normal) on the Age-Related Eye Disease Study 9-step AMD classification system based on color fundus photographs graded by experienced and masked evaluators.

METHODS: Rod-mediated DA was assessed at baseline in 1 eye after a photobleach using a computerized dark adaptometer with targets centered at 5° on the inferior vertical meridian. Speed of DA was characterized by the rod-intercept value, with abnormal DA defined as rod-intercept ≥12.3 minutes. Demographic characteristics, best-corrected visual acuity, and smoking status were also assessed. Log-binomial regression was used to calculate unadjusted and adjusted risk ratios (RRs) and associated 95% confidence intervals (CIs) for the association between baseline DA and incident AMD.

MAIN OUTCOME MEASURES: Presence of AMD at the 3-year follow-up visit for the eye tested for DA at baseline.

RESULTS: Both baseline and follow-up visits were completed by 325 persons (mean age, 67.8 years). At baseline, 263 participants had normal DA with mean rod-intercept of 9.1 (standard deviation [SD], 1.5), and 62 participants had abnormal DA with mean rod-intercept of 15.1 (SD, 4.0). After adjustment for age and smoking, those with abnormal DA in the tested eye at baseline were approximately 2 times more likely to have AMD in that eye (RR, 1.92; 95% CI, 1.03-3.62) by the time of the follow-up visit, compared with those who had normal DA at baseline.

CONCLUSIONS: Delayed rod-mediated DA in older adults with normal macular health is associated with incident early AMD 3 years later, and thus is a functional biomarker for early disease. The biological relevance of this test is high, because it assesses translocation of vitamin A derivatives across the retinal pigment epithelium and Bruch's membrane, 2 tissues with prominent age- and AMD-related pathology.

PMID: 26522707 [PubMed - as supplied by publisher]

Ophthalmology. 2015 Nov 3. [Epub ahead of print]

Natural History of Geographic Atrophy Progression Secondary to Age-Related Macular Degeneration (Geographic Atrophy Progression Study).

Schmitz-Valckenberg S, Sahel JA, Danis R, Fleckenstein M, Jaffe GJ, Wolf S, Pruente C, Holz FG.

PURPOSE: The Geographic Atrophy Progression (GAP) study was designed to assess the rate of geographic atrophy (GA) progression and to identify prognostic factors by measuring the enlargement of the atrophic lesions using fundus autofluorescence (FAF) and color fundus photography (CFP).

DESIGN: Prospective, multicenter, noninterventional natural history study.

PARTICIPANTS: A total of 603 participants were enrolled in the study; 413 of those had gradable lesion data from FAF or CFP, and 321 had gradable lesion data from both FAF and CFP.

METHODS: Atrophic lesion areas were measured by FAF and CFP to assess lesion progression over time. Lesion size assessments and best-corrected visual acuity (BCVA) were conducted at screening/baseline (day 0) and at 3 follow-up visits: month 6, month 12, and month 18 (or early exit).

MAIN OUTCOME MEASURES: The GA lesion progression rate in disease subgroups and mean change from baseline visual acuity.

RESULTS: Mean (standard error) lesion size changes from baseline, determined by FAF and CFP, respectively, were 0.88 (0.1) and 0.78 (0.1) mm2 at 6 months, 1.85 (0.1) and 1.57 (0.1) mm2 at 12 months, and 3.14 (0.4) and 3.17 (0.5) mm2 at 18 months. The mean change in lesion size from baseline to month 12 was significantly greater in participants who had eyes with multifocal atrophic spots compared with those with unifocal spots ($P < 0.001$) and those with extrafoveal lesions compared with those with foveal lesions ($P = 0.001$). The mean (standard deviation) decrease in visual acuity was 6.2 ± 15.6 letters for patients with image data available. Atrophic lesions with a diffuse (mean 0.95 mm2) or banded (mean 1.01 mm2) FAF pattern grew more rapidly by month 6 compared with those with the "none" (mean, 0.13 mm2) and focal (mean, 0.36 mm2) FAF patterns.

CONCLUSIONS: Although differences were observed in mean lesion size measurements using FAF imaging compared with CFP, the measurements were highly correlated with one another. Significant differences were found in lesion progression rates in participants stratified by hyperfluorescence pattern subtype. This large GA natural history study provides a strong foundation for future clinical trials.

PMID: 26545317 [PubMed - as supplied by publisher]

Sci Rep. 2015 Nov 6;5:16204.

Pachychoroid neovasculopathy and age-related macular degeneration.

Miyake M, Ooto S, Yamashiro K, Takahashi A, Yoshikawa M, Akagi-Kurashige Y, Ueda-Arakawa N, Oishi A, Nakanishi H, Tamura H, Tsujikawa A, Yoshimura N.

Abstract: Pachychoroid neovasculopathy is a recently proposed clinical entity of choroidal neovascularization (CNV). As it often masquerades as neovascular age-related macular degeneration (AMD), it is currently controversial whether pachychoroid neovasculopathy should be distinguished from neovascular AMD. This is because its characteristics have yet to be well described. To estimate the relative prevalence of pachychoroid neovasculopathy in comparison with neovascular AMD and to investigate the phenotypic/genetic differences of the two diseases, we evaluated 200 consecutive Japanese patients who agreed to participate in the genetic study and diagnosed with pachychoroid neovasculopathy or neovascular AMD. Pachychoroid neovasculopathy was observed in 39 individuals (19.5%), which corresponds to one fourth of neovascular AMD. Patients with pachychoroid neovasculopathy were significantly younger ($p = 5.1 \times 10(-5)$) and showed a greater subfoveal choroidal thickness ($p = 3.4 \times 10(-$

14)). Their genetic susceptibility to AMD was significantly lower than that of neovascular AMD; ARMS2 rs10490924 (p = 0.029), CFH rs800292 (p = 0.013) and genetic risk score calculated from 11 AMD susceptibility genes (p = 3.8 × 10(-3)). Current results implicate that the etiologies of the two conditions must be different. Thus, it will be necessary to distinguish these two conditions in future studies.

PMID: 26542071 [PubMed - in process]

Retin Cases Brief Rep. 2015 Nov 3. [Epub ahead of print]

TREATMENT OF RETINOPATHY AND MACULAR EDEMA SECONDARY TO A CAROTID-CAVERNOUS FISTULA.

Roybal CN, Kucukevcilioglu M, Huckfeldt R, Elshatory Y, Thurtell MJ, Folk JC.

PURPOSE: To present a case report on a patient with retinal complications from a carotid-cavernous fistula.

METHODS: Observational case report.

RESULTS: A 26-year-old patient sustained head trauma following a motorcycle accident. Examination and retinal imaging demonstrated a venous stasis retinopathy with cystoid macular edema. The edema resolved with aflibercept, but not with bevacizumab.

CONCLUSION: The patient was diagnosed with venous stasis retinopathy secondary to carotid-cavernous fistula. Pathologic findings completely resolved with appropriate management.

PMID: 26536012 [PubMed - as supplied by publisher]

J Toxicol Pathol. 2015 Oct;28(4):181-8. Epub 2015 Jul 27.

Characteristics of structures and lesions of the eye in laboratory animals used in toxicity studies.

Shibuya K, Tomohiro M, Sasaki S, Otake S.

Abstract: Histopathology of the eye is an essential part of ocular toxicity evaluation. There are structural variations of the eye among several laboratory animals commonly used in toxicity studies, and many cases of ocular lesions in these animals are related to anatomical and physiological characteristics of the eye. Since albino rats have no melanin in the eye, findings of the fundus can be observed clearly by ophthalmoscopy. Retinal atrophy is observed as a hyper-reflective lesion in the fundus and is usually observed as degeneration of the retina in histopathology. Albino rats are sensitive to light, and light-induced retinal degeneration is commonly observed because there is no melanin in the eye. Therefore, it is important to differentiate the causes of retinal degeneration because the lesion occurs spontaneously and is induced by several drugs or by lighting. In dogs, the tapetum lucidum, a multilayered reflective tissue of the choroid, is one of unique structures of the eye. Since tapetal cells contain reflecting crystals in which a high level of zinc has been demonstrated chemically, drug-induced tapetum degeneration is possibly related to zinc chelation. The eye of the monkey has a macula similar to that of humans. The macula consists only of cones with a high density, and light falls directly on the macula that plays an important role in visual acuity. Macular degeneration occurring in monkeys resembles histopathologically that of humans. Hence, the eye of the monkey is a suitable model to investigate macular degeneration and to assess drug-induced macular lesions.

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Pathogenesis

Trans Am Ophthalmol Soc. 2015 Sep;113:T51-T522.

Lipoprotein(A) with An Intact Lysine Binding Site Protects the Retina From an Age-Related Macular Degeneration Phenotype in Mice (An American Ophthalmological Society Thesis).

Handa JT, Tagami M, Ebrahimi K, Leibundgut G, Janiak A, Witztum JL, Tsimikas S.

PURPOSE: To test the hypothesis that the accumulation of oxidized phospholipids (OxPL) in the macula is toxic to the retina unless neutralized by a variety of mechanisms, including binding by lipoprotein(a) [Lp(a)], which is composed of apolipoprotein(a) [apo(a)] and apolipoprotein B-100 (apoB).

METHODS: Human maculas and eyes from two Lp(a) transgenic murine models were subjected to morphologic, ultrastructural, and immunohistochemical analysis. "Wild-type Lp(a)" mice, which express human apoB-100 and apo(a) that contains oxidized phospholipid, and "mutant LBS(-) Lp(a)" mice with a defective apo(a) lysine binding site (LBS) for oxidized phospholipid binding, were fed a chow or high-fat diet for 2 to 12 months. Oxidized phospholipid-containing lipoproteins were detected by immunoreactivity to E06, a murine monoclonal antibody binding to the phosphocholine headgroup of oxidized, but not native, phospholipids.

RESULTS: Oxidized phospholipids, apo(a), and apoB accumulate in maculas, including drusen, of age-related macular degeneration (AMD) samples and age-matched controls. Lp(a) mice fed a high-fat diet developed age-related changes. However, mutant LBS(-) Lp(a) mice fed a high-fat diet developed retinal pigment epithelial cell degeneration and drusen. These changes were associated with increased OxPL, decreased antioxidant defenses, increased complement, and decreased complement regulators.

CONCLUSIONS: Human maculas accumulate Lp(a) and OxPL. Mutant LBS(-) Lp(a) mice, lacking the ability to bind E06-detectable oxidized phospholipid, develop AMD-like changes. The ability of Lp(a) to bind E06-detectable OxPL may play a protective role in AMD.

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J Hypertens. 2015 Dec;33(12):2382-8. doi: 10.1097/HJH.0000000000000766.

Essential hypertension in the pathogenesis of age-related macular degeneration: a review of the current evidence.

Katsi VK1, Marketou ME, Vrachatis DA, Manolis AJ, Nihoyannopoulos P, Tousoulis D, Vardas PE, Kallikazaros I.

Abstract: Age-related macular degeneration (AMD) is one of the main causes of vision loss, especially in the elderly. The involvement of essential hypertension in its pathogenesis has been well covered in the literature since it was first recognized. Hemodynamic abnormalities appear to contribute to AMD, with the renin-angiotensin system playing a significant role. Many studies have demonstrated that high blood pressure is associated with lower choroidal blood flow and disturbed vascular homeostasis in these patients. In addition, AMD is characterized by abnormal neovascularization, to which angiotensin II and growth factors make a large contribution. Most epidemiological studies have found essential hypertension to be a risk factor for AMD. However, although all agree that the strongest predisposing factors are age and smoking, overall there is some inconsistency regarding the exact role of hypertension in its pathogenesis. In particular, there are no data in the literature to support the view that antihypertensive medication and the successful management of hypertension have a positive effect on the clinical outcome of AMD. This reinforces the data indicating that the cause of AMD is multifactorial and suggests that, although essential hypertension probably plays a role, in itself it is unlikely to be a major contributor to the future occurrence of AMD.

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Invest Ophthalmol Vis Sci. 2015 Nov 1;56(12):7137-45.

Phosphatidylserine (PS) Is Exposed in Choroidal Neovascular Endothelium: PS-Targeting Antibodies Inhibit Choroidal Angiogenesis In Vivo and Ex Vivo.

Li T, Aredo B, Zhang K, Zhong X, Pulido JS, Wang S, He YG, Huang X, Brekken RA, Ufret-Vincenty RL.

PURPOSE: Choroidal neovascularization (CNV) accounts for 90% of cases of severe vision loss in patients with advanced age-related macular degeneration. Identifying new therapeutic targets for CNV may lead to novel combination therapies to improve outcomes and reduce treatment burden. Our goal was to test whether phosphatidylserine (PS) becomes exposed in the outer membrane of choroidal neovascular endothelium, and whether this could provide a new therapeutic target for CNV.

METHODS: Choroidal neovascularization was induced in C57BL/6J mice using laser photocoagulation. Choroidal neovascularization lesions costained for exposed PS and for intercellular adhesion molecule 2 (or isolectin B4) were imaged in flat mounts and in cross sections. The laser CNV model and a choroidal sprouting assay were used to test the effect of PS-targeting antibodies on choroidal angiogenesis. Choroidal neovascularization lesion size was determined by intercellular adhesion molecule 2 (ICAM-2) staining of flat mounts.

RESULTS: We found that PS was exposed in CNV lesions and colocalized with vascular endothelial staining. Treatment with PS-targeting antibodies led to a 40% to 80% reduction in CNV lesion area when compared to treatment with a control antibody. The effect was the same as that seen using an equal dose of an anti-VEGF antibody. Results were confirmed using the choroid sprouting assay, an ex vivo model of choroidal angiogenesis.

CONCLUSIONS: We demonstrated that PS is exposed in choroidal neovascular endothelium. Furthermore, targeting this exposed PS with antibodies may be of therapeutic value in CNV.

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Cell Stem Cell. 2015 Oct 28. [Epub ahead of print]

Histone Demethylase Expression Enhances Human Somatic Cell Nuclear Transfer Efficiency and Promotes Derivation of Pluripotent Stem Cells.

Chung YG, Matoba S, Liu Y, Eum JH, Lu F, Jiang W, Lee JE, Sepilian V, Cha KY, Lee DR, Zhang Y.

Abstract: The extremely low efficiency of human embryonic stem cell (hESC) derivation using somatic cell nuclear transfer (SCNT) limits its potential application. Blastocyst formation from human SCNT embryos occurs at a low rate and with only some oocyte donors. We previously showed in mice that reduction of histone H3 lysine 9 trimethylation (H3K9me3) through ectopic expression of the H3K9me3 demethylase Kdm4d greatly improves SCNT embryo development. Here we show that overexpression of a related H3K9me3 demethylase KDM4A improves human SCNT, and that, as in mice, H3K9me3 in the human somatic cell genome is an SCNT reprogramming barrier. Overexpression of KDM4A significantly improves the blastocyst formation rate in human SCNT embryos by facilitating transcriptional reprogramming, allowing efficient derivation of SCNT-derived ESCs using adult Age-related Macular Degeneration (AMD) patient somatic nuclei donors. This conserved mechanistic insight has potential applications for improving SCNT in a variety of contexts, including regenerative medicine.

PMID: 26526725 [PubMed - as supplied by publisher]

Cell Mol Neurobiol. 2015 Nov 2. [Epub ahead of print]

Expression of Aquaporin-6 in Rat Retinal Ganglion Cells.

Jang SY, Lee ES, Ohn YH, Park TK.

Abstract: Several aquaporins (AQPs) have been identified to be present in the eyes, and it has been suggested that they are involved in the movement of water and small solutes. AQP6, which has low water permeability and transports mainly anions, was recently discovered in the eyes. In the present study, we investigate the localization of AQP6 in the rat retina and show that AQP6 is selectively localized to the ganglion cell layer and the outer plexiform layer. Along with the gradual decrease in retinal ganglion cells after a crushing injury of optic nerve, immunofluorescence signals of AQP6 gradually decreased. Confocal microscope images confirmed AQP6 expression in retinal ganglion cells and Müller cells in vitro. Therefore, AQP6 might participate in water and anion transport in these cells.

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Am J Med. 2015 Oct 30. [Epub ahead of print]

Mining Retrospective Data for Virtual Prospective Drug Repurposing: L-DOPA and Age-related Macular Degeneration.

Brilliant MH, Vaziri K, Connor TB Jr, Schwartz SG, Carroll JJ, McCarty CA, Schrodi SJ, Hebbring SJ, Kishor KS, Flynn HW Jr, Moshfeghi AA, Moshfeghi DM, Fini ME, McKay BS.

BACKGROUND: Age-related Macular Degeneration (AMD) is a leading cause of visual loss among the elderly. A key cell-type involved in AMD, the retinal pigment epithelium expresses a g-protein coupled receptor that, in response to its ligand, L-DOPA, upregulates pigment epithelia derived factor, while downregulating vascular endothelial growth factor. In this study we investigated the potential relationship between L-DOPA and AMD.

METHODS: We used retrospective analysis to compare the incidence of AMD between patients taking vs. not taking L-DOPA. We analyzed 2 separate cohorts of patients with extensive medical records from the Marshfield Clinic (~17,000 and ~20,000) and the Truven MarketScan outpatient and databases (~87 million) patients. We used ICD-9 codes to identify AMD diagnoses and L-DOPA prescriptions to determine the relative risk of developing AMD and age of onset with or without an L-DOPA prescription.

RESULTS: In the retrospective analysis of patients without an L-DOPA prescription, AMD age of onset was 71.2, 71.3 and 71.3 in three independent retrospective cohorts. AMD occurred significantly later in patients with an L-DOPA prescription, 79.4 in all cohorts. The odds ratio of developing AMD was also significantly negatively correlated by L-DOPA (OR=0.78;CI=0.76-0.80;P<0.001). Similar results were observed for neovascular AMD, p<0.001.

CONCLUSION: Exogenous L-DOPA was protective against AMD. L-DOPA is normally produced in pigmented tissues such as the retinal pigment epithelium as a byproduct of melanin synthesis by tyrosinase. GPR143 is the only known L-DOPA receptor, it is therefore plausible that GPR143 may be a fruitful target to combat this devastating disease.

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Artif Cells Nanomed Biotechnol. 2015 Nov 2:1-10. [Epub ahead of print]

Cytotoxic effect of ZnS nanoparticles on primary mouse retinal pigment epithelial cells.

Bose K, Lakshminarasimhan H, Sundar K, Kathiresan T.

Abstract: The multiple properties of zinc sulphide nanoparticles (ZnS-NPs) are attracting great attention in the field of chemical and biological research. ZnS-NPs also find their application in biosensor and photocatalysis. Zinc is an important metal ion in retina and its deficiency leads to age-related macular degeneration. As of now, not much research is available on bio-interaction of ZnS as nanoform with retinal pigment epithelial (RPE) cells. RPE cells in the retina help in maintaining normal photoreceptor function and vision. To begin with, ZnS-NPs were synthesized and characterized using UV-visible spectra, X-ray

diffraction, Fourier transform infrared spectrum, transmission electron microscopy and dynamic light scattering. Followed by the confirmation of nanoparticles, our study extended to investigate the impact of ZnS-NPs in primary mouse RPE (MRPE) cells at different concentrations. ZnS-NPs showed dose-dependent cytotoxicity in MRPE cells and no changes were observed in cells' tight intactness at minimal concentration. In addition, exposure to ZnS-NPs increased cellular permeability in dose- and time-dependent manner in MRPE cells. The findings from DCFH-DA analysis revealed that ZnS-NPs-treated cells had elevated level of reactive oxygen species and partial activation of cell apoptosis was identified after exposure to ZnS-NPs at higher concentration. Furthermore, pre-treatment of the primary MRPE cells with ZnS-NPs led to phosphorylation of Akt (Ser 473), which indicates the crucial role of ZnS-NPs in regulating cell survival at minimal concentration. Altogether, this study enumerates requisite dose of using ZnS-NPs to maintain healthy RPE cells and contributes to future studies in development of therapeutic drug and drug carrier for ocular-related disorders.

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Pharmacol Res. 2015 Oct 30. [Epub ahead of print]

Pharmacology of the cell/matrix form of adhesion.

Meldolesi J.

Abstract: Cell adhesions are heterogeneous processes including two main forms, CAM and cell/matrix forms. Both these forms induce the interaction among cells and with the extracellular matrix, and the generation of intracellular signals. The signaling of the two adhesion forms include, at the cell surface, involvement of distinct integrins, necessary for intracellular cascade activation. I will focus on the cell/integrin form based on two specific integrins, α5β1 (the most important) and αvβ3, activated by the preferential binding of fibronectin, a unique extracellular matrix protein. Such binding induces local assembly of stratified adhesion complexes containing protein kinases, that trigger the intracellular signaling cascades (Akt, ERK and others); proteins that sustain mechanical processes; and proteins associated with the cytoskeleton. In view of its role in several diseases, from cancers to the eye macular-degeneration; from brain neurodegeneration to fibroses, the pharmacological interest for the cell/integrin adhesion has grown, and presumably will further grow in the near future. The agents identified and developed for therapy include antibodies, many peptides and chemical drugs against α5β1 integrin; drugs against fibronectin and metalloproteinases 2/9, responsible of the latter enzyme proteolysis; anti-kinase and anti-cascade drugs, some of which targeted to the activation of transcription factors and/or their transfer to the nucleus, with repression or activation of gene expression. A new perspective, based on the investigation of both animal models and human patients, includes factors active on the cell/matrix and CAM adhesions, considered separately or coordinately in distinct therapeutic approaches, integrated or not with classical chemotherapic treatments.

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Stem Cells. 2015 Nov 2. [Epub ahead of print]

Human umbilical tissue-derived cells rescue retinal pigment epithelium dysfunction in retinal degeneration.

Cao J, Murat C, An W, Yao X, Lee J, Santulli-Marotto S, Harris IR, Inana G.

Abstract: Retinal pigment epithelium (RPE) cells perform many functions crucial for retinal preservation and vision. RPE cell dysfunction results in various retinal degenerative diseases, such as retinitis pigmentosa and age-related macular degeneration (AMD). Currently, there are no effective treatments for retinal degeneration except for a small percentage of individuals with exudative AMD. Cell therapies targeting RPE cells are being developed in the clinic for the treatment of retinal degeneration. Subretinal injection of human umbilical tissue-derived cells (hUTC) in the Royal College of Surgeons (RCS) rat model of retinal

degeneration was shown to preserve photoreceptors and visual function. However, the precise mechanism remains unclear. Here, we demonstrate that hUTC rescue phagocytic dysfunction in RCS RPE cells in vitro. hUTC secrete receptor tyrosine kinase (RTK) ligands brain-derived neurotrophic factor (BDNF), hepatocyte growth factor (HGF), and glial cell-derived neurotrophic factor (GDNF), as well as opsonizing bridge molecules milk-fat-globule-EGF-factor 8 (MFG-E8), growth arrest-specific 6 (Gas6), thrombospondin (TSP)-1, and TSP-2. The effect of hUTC on phagocytosis rescue in vitro was mimicked by recombinant human proteins of these factors and was abolished by siRNA-targeted gene silencing in hUTC. The bridge molecules secreted from hUTC bound to the photoreceptor outer segments and facilitated their ingestion by the RPE. This study elucidates novel cellular mechanisms for the repair of RPE function in retinal degeneration through RTK ligands and bridge molecules, and demonstrates the potential of using hUTC for the treatment of retinal degenerative diseases.

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Epidemiology

Ann Neurosci. 2015 Oct;22(4):232-7.

Exploring the role of VEGF in Indian Age related macular degeneration.

Sharma K, Sharma NK, Singh R, Anand A.

BACKGROUND: Age related macular degeneration (AMD) is major devastating neurodegenerative disorder characterized by progressive irreversible vision loss in the elderly persons. In spite of several genetic and environmental factors, the role of VEGF and CFH predispose the pathological phenomenon in the AMD patients.

PURPOSE: The aim of the study was to estimate the VEGF levels in the serum of AMD patients and its correlation with co-morbidity of the participants.

METHODS: The study recruited the 98 AMD patients and 59 controls with proper consent of the participants as per the exclusion-inclusion criteria. The co-morbidity and socio-economic details were obtained by introducing the standard questionnaire amongst the participants. Serum levels of vascular endothelial growth factor (VEGF) was estimated by ELISA and compared with the control population of the study. The levels of VEGF in the serum of AMD patients and controls were compared with Mann-Whitney U -test. Kruskal Wallis one-way analysis of variance (ANOVA) was employed to analyze more than two variables in the study.

RESULTS: Elevated level of VEGF was found in AMD patients as compared to controls. Surprisingly, we did not find significant changes among wet AMD subtypes i.e. minimal, predominant and classic wet AMD. However, we have demonstrated the intravitreal anti-VEGF treatment (avastin) in AMD patients could reduce the systemic VEGF levels although it was not significant. Moreover, the heart ailment in the AMD patients could also influence the VEGF levels.

CONCLUSION: Our study is consistent with previous studies describing the imperative significance of VEGF in AMD pathology. However, our study did not reveal the role of VEGF in wet AMD progression but it is well established causative agent for the same. The increased levels of VEGF in heart ailment among AMD patients are significant.

PMID: 26526736 [PubMed] PMCID: PMC4627204

Diet, lifestyle & low vision

Prog Retin Eye Res. 2015 Nov 2. [Epub ahead of print]

Lutein, zeaxanthin, and meso-zeaxanthin: The basic and clinical science underlying carotenoid-based nutritional interventions against ocular disease.

Bernstein PS, Li B, Vachali PP, Gorusupudi A, Shyam R, Henriksen BS, Nolan JM.

Abstract: The human macula uniquely concentrates three carotenoids: lutein, zeaxanthin, and meso-zeaxanthin. Lutein and zeaxanthin must be obtained from dietary sources such as green leafy vegetables and orange and yellow fruits and vegetables, while meso-zeaxanthin is rarely found in diet and is believed to be formed at the macula by metabolic transformations of ingested carotenoids. Epidemiological studies and large-scale clinical trials such as AREDS2 have brought attention to the potential ocular health and functional benefits of these three xanthophyll carotenoids consumed through the diet or supplements, but the basic science and clinical research underlying recommendations for nutritional interventions against age-related macular degeneration and other eye diseases are underappreciated by clinicians and vision researchers alike. In this review article, we first examine the chemistry, biophysics, and physiology of these yellow pigments that are specifically concentrated in the macula lutea through the means of high-affinity binding proteins and specialized transport and metabolic proteins where they play important roles as short-wavelength (blue) light-absorbers and localized, efficient antioxidants in a region at high risk for light-induced oxidative stress. Next, we turn to clinical evidence supporting functional benefits of these carotenoids in normal eyes and for their potential protective actions against ocular disease from infancy to old age.

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Ann Neurosci. 2015 Oct;22(4):239-43.

Milk metabolites and neurodegeneration: Is there crosstalk?

Thakur K, Anand A.

Abstract: Milk has been considered as a natural source of nutrition for decades. Milk is known to be nutrient -rich which aids the growth and development of the human body. Milk contains both macro- and micronutrients. Breast milk is widely regarded as the optimal source of neonatal nutrition due to its composition of carbohydrates, proteins, minerals and antibodies. However, despite the wide use of milk products, investigations into the role of milk in degenerative diseases have been limited. This review will examine the relationship between the β-casein gene found in bovine milk and disease states by using age-related macular degeneration as an example.

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