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MD Research News

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Drug treatment

Ophthalmic Surg Lasers Imaging Retina. 2014 Jul 1;45(4):285-91. doi: 10.3928/23258160-20140709-04.

Clinical monitoring of patients with age-related macular degeneration treated with intravitreal bevacizumab or ranibizumab.

Kiss S, Liu Y, Brown J, Holekamp NM, Almony A, Campbell J, Kowalski JW.

BACKGROUND AND OBJECTIVE: Patients with neovascular age-related macular degeneration (AMD) require frequent follow-up and regular anti-VEGF injections for optimal outcomes. Although studies suggest that injection frequency is suboptimal in clinical practice, monitoring frequency in this setting is unclear. This study evaluates annual monitoring patterns between 2008 and 2011.

PATIENTS AND METHODS: This retrospective claims analysis included newly diagnosed neovascular AMD patients with at least one intravitreal bevacizumab or ranibizumab injection (8,811 and 2,877 patients, respectively). Patient monitoring and treatment patterns were assessed at 12-month intervals.

RESULTS: From 2008 to 2010, the mean number of injections increased. In the 2010 cohort, among bevacizumab- and ranibizumab-treated patients, respectively, less than 23% and less than 40% had at least 10 ophthalmologist visits, and less than 4% and less than 21% had at least 10 optical coherence tomography scans.

CONCLUSION: Patients with neovascular AMD in clinical settings during 2008 to 2011 were monitored less frequently and received fewer anti-VEGF injections than patients in major clinical trials, which may affect outcomes. [Ophthalmic Surg Lasers Imaging Retina. 2014;45:285-291.].

PMID: 25037010 [PubMed - in process]

Ophthalmic Surg Lasers Imaging Retina. 2014 Jul 1;45(4):275-81. doi: 10.3928/23258160-20140709-03.

Intravitreal bevacizumab and aflibercept for the treatment of exudative age-related macular degeneration.

Selid PD, Jundt MC, Fortney AC, Beal JR.

BACKGROUND AND OBJECTIVE: To compare treatment of exudative age-related macular degeneration

(AMD) with bevacizumab versus aflibercept in terms of central retinal thickness (CRT) and best corrected visual acuity (BCVA).

PATIENTS AND METHODS: A retrospective cohort study examining changes in CRT and BCVA over 12 months of follow-up in 111 patients treated with bevacizumab and 91 treated with aflibercept for exudative AMD.

RESULTS: Treatment with bevacizumab and aflibercept reduced CRT from baseline to 12 months. Aflibercept significantly reduced the mean change from baseline CRT at 12 months compared to bevacizumab. However, mean CRT at 12 months was not significantly different after aflibercept versus bevacizumab (271.6 ± 74.0 μm vs 257.9 ± 48.5 μm). BCVA was significantly better at 6 months in the aflibercept group. At baseline, 18.5% of bevacizumab and 26.4% of aflibercept patients had BCVA better than 20/40. At 12 months, 34.8% of bevacizumab and 38.9% of aflibercept patients had BCVA better than 20/40.

CONCLUSION: CRT decreased and BCVA improved after treatment with bevacizumab and aflibercept for exudative AMD.

PMID: 25037009 [PubMed - in process]

Br J Ophthalmol. 2014 Jul 17. pii: bjophthalmol-2014-305105. doi: 10.1136/bjophthalmol-2014-305105. [Epub ahead of print]

Effects of aflibercept on primary RPE cells: toxicity, wound healing, uptake and phagocytosis.

Klettner A, Tahmaz N, Dithmer M, Richert E, Roider J.

BACKGROUND/AIM: Anti-VEGF treatment is the therapy of choice in age-related macular degeneration, and is also applied in diabetic macular oedema or retinal vein occlusion. Recently, the fusion protein, aflibercept, has been approved for therapeutic use. In this study, we investigate the effects of aflibercept on primary RPE cells.

METHODS: Primary RPE cells were prepared from freshly slaughtered pigs' eyes. The impact of aflibercept on cell viability was investigated with MTT and trypan blue exclusion assay. The influence of aflibercept on wound healing was assessed with a scratch assay. Intracellular uptake of aflibercept was investigated in immunohistochemistry and its influence on phagocytosis with a phagocytosis assay using opsonised latex beads.

RESULTS: Aflibercept displays no cytotoxicity on RPE cells but impairs its wound healing ability. It is taken up into RPE cells and can be intracellularly detected for at least 7 days. Intracellular aflibercept impairs the phagocytic capacity of RPE cells.

CONCLUSIONS: Aflibercept interferes with the physiology of RPE cells, as it is taken up into RPE cells, which is accompanied by a reduction of the phagocytic ability. Additionally, it impairs the wound healing capacity of RPE cells. These effects on the physiology of RPE cells may indicate possible side effects.

PMID: 25034050 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2014 Jul 17. [Epub ahead of print]

Evaluation of plasma vascular endothelial growth factor levels after intravitreal injection of ranibizumab and aflibercept for exudative age-related macular degeneration.

Yoshida I, Shiba T, Taniguchi H, Takahashi M, Murano T, Hiruta N, Hori Y, Bujo H, Maeno T.

BACKGROUND: To evaluate the plasma vascular endothelial growth factor (VEGF) levels after one intravitreal injection of aflibercept or ranibizumab in patients with exudative age-related macular degeneration (AMD).

METHODS: Twenty-four Japanese with exudative AMD, polypoidal choroidal vasculopathy, and retinal angiomatous proliferation were included. Fourteen patients received an intravitreal injection of aflibercept, and ten patients received an intravitreal injection of ranibizumab. Plasma VEGF levels were evaluated within 7 days before the intravitreal injections and 1 day, 1 week, and 1 month after the intravitreal injection.

RESULTS: In the ranibizumab group, the mean plasma VEGF levels were 245.7 ± 233.4 pg/ml before the injection, 246.6 ± 304.8 pg/ml after 1 day, 217.8 ± 212.9 pg/ml after 1 week, and 260.0 ± 290.1 pg/ml after 1 month. The plasma VEGF levels did not decrease significantly in patients in the ranibizumab group at any time point. In the aflibercept group, the mean plasma VEGF levels were 280.0 ± 170.3 pg/ml before the intravitreal injection and 8.2 ± 12.9 pg/ml after 1 day, 9.1 ± 9.1 pg/ml after 1 week, and 41.9 ± 41.4 pg/ml after 1 month ($p < 0.0001$, vs before injection).

CONCLUSION: Intravitreally injected aflibercept reduced plasma VEGF over at least 1 month. In contrast, intravitreal injection of ranibizumab did not cause a significant reduction in the plasma VEGF levels.

PMID: 25030237 [PubMed - as supplied by publisher]

PLoS One. 2014 Jul 16;9(7):e102309. doi: 10.1371/journal.pone.0102309. eCollection 2014.

Efficacy of Anti-VEGF and Laser Photocoagulation in the Treatment of Visual Impairment due to Diabetic Macular Edema: A Systematic Review and Network Meta-Analysis.

Régnier S, Malcolm W, Allen F, Wright J, Bezlyak V.

OBJECTIVE: Compare the efficacy of ranibizumab, aflibercept, laser, and sham in the first-line treatment of diabetic macular edema (DME) to inform technology assessments such as those conducted by the UK National Institute for Health and Care Excellence (NICE).

DATA SOURCES: MEDLINE, Embase, Cochrane Library, congress abstracts, ClinicalTrials.gov registry and Novartis data on file.

INCLUSION CRITERIA: Studies reporting 6- or 12-month results of randomized controlled trials (RCTs) evaluating at least two of ranibizumab 0.5 mg pro re nata, aflibercept 2.0 mg bi-monthly, laser photocoagulation or sham. Study quality was assessed based on likelihood of bias in selection, attrition, detection and performance.

OUTCOME MEASURE: Improvement in best-corrected visual acuity (BCVA) measured as the proportion of patients gaining ≥10 letters on the Early Treatment Diabetic Retinopathy Study scale. The outcome was chosen following acceptance by NICE of a Markov model with 10-letter health states in the assessment of ranibizumab for DME.

META-ANALYSIS: Bayesian network meta-analyses with fixed and random effects adjusted for differences in baseline BCVA or central retinal thickness.

RESULTS: The analysis included 1,978 patients from eight RCTs. The random effects model adjusting for baseline BCVA was the best model based on total residual. The efficacy of ranibizumab was numerically, but not statistically, superior to aflibercept (odds ratio [OR] 1.59; 95% credible interval [CrI], 0.61-5.37). Ranibizumab and aflibercept were statistically superior to laser monotherapy with ORs of 5.50 (2.73-13.16) and 3.45 (1.62-6.84) respectively. The probability that ranibizumab is the most efficacious treatment was 73% compared with 14% for aflibercept, 12% for ranibizumab plus laser, and 0% for laser.

LIMITATIONS: Three of the eight RCTs included are not yet published. The models did not adjust for all

potential effect modifiers.

CONCLUSION: Ranibizumab was non-significantly superior to aflibercept and both anti-VEGF therapies had statistically superior efficacy to laser.

PMID: 25029255 [PubMed - in process]

Clin Ophthalmol. 2014 Jun 24;8:1199-202. doi: 10.2147/OPTH.S65810. eCollection 2014.

Effect of intravitreal aflibercept injection for age-related macular degeneration with a retinal pigment epithelial tear refractory to intravitreal ranibizumab injection.

Fujii A, Imai H, Kanai M, Azumi A.

BACKGROUND: The purpose of this study was to evaluate the effects of intravitreal aflibercept injection for age-related macular degeneration (AMD) with a retinal pigment epithelial (RPE) tear after intravitreal ranibizumab injection (IVR) which finally became resistant to additional IVR.

METHODS: We reviewed the medical records of AMD patients with RPE tears after intravitreal ranibizumab injection who were treated with intravitreal aflibercept injection after acquisition of resistance to additional IVR.

RESULTS: One eye from three patients, aged 66, 77, and 78 years, was evaluated. All cases started treatment with IVR for AMD. RPE tear developed 1, 4, and 3 months after the first IVR, respectively. Additional IVR was performed seven, seven, and nine times over 10, 19, and 21 months, respectively, but all cases finally became resistant to IVR. Intravitreal aflibercept injection was performed four times, six times, and once over 8, 9, and 6 months, respectively. At the last visit, all patients had complete resolution of subretinal and intraretinal fluid.

CONCLUSION: Continued intravitreal aflibercept injection may be beneficial to manage AMD with RPE tear which has become resistant to additional IVR.

PMID: 25028532 [PubMed] PMCID: PMC4077850

Ophthalmology. 2014 Jul 12. pii: S0161-6420(14)00486-2. doi: 10.1016/j.ophtha.2014.05.022. [Epub ahead of print]

Systemic Vascular Safety of Ranibizumab for Age-related Macular Degeneration: Systematic Review and Meta-analysis of Randomized Trials.

Ueta T, Noda Y, Toyama T, Yamaguchi T, Amano S.

BACKGROUND: We conducted a meta-analysis of randomized trials of ranibizumab for age-related macular degeneration (AMD) to elucidate systemic vascular risk.

CLINICAL RELEVANCE: Although intravitreal vascular endothelial growth factor inhibitors are widely used to treat AMD, whether they produce systemic adverse effects remains uncertain.

METHODS: We searched MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials through March 2014 to identify the randomized trials that compared systemic safety among different intensities of ranibizumab treatment for AMD. The outcome measures were the incidence of cerebrovascular accidents (CVAs), myocardial infarctions, nonocular hemorrhages, overall arterial thromboembolic events (ATEs), and all-cause mortality. We calculated the Peto odds ratio (OR) with 95% confidence interval for the comparisons between different intensities of regimens in terms of dose and retreatment frequency.

RESULTS: Eleven trials comprising 6596 patients with AMD were included in the meta-analysis. A

significant increase was observed in the following comparisons: 0.5 versus 0.3/0.0 mg for CVA (OR, 1.86; 95% CI, 1.05-3.29; P = 0.03), monthly versus pro re nata (PRN)/0.0 mg for CVA (OR, 1.89; 95% CI, 1.06-3.38; P = 0.03), and 0.3/0.5 versus 0.0 mg for nonocular hemorrhage (OR, 1.57; 95% CI, 1.01-2.44; P = 0.04). A nonsignificant increase was observed in the following comparisons: 0.5 versus 0.0 mg for CVA (OR, 2.27; 95% CI, 0.90-5.69; P = 0.08), monthly versus PRN for CVA (OR, 2.04; 95% CI, 0.94-4.45; P = 0.07), 0.5 versus 0.0 mg for nonocular hemorrhage (OR, 1.68; 95% CI, 0.98-2.88; P = 0.06), 0.3 versus 0.0 mg for nonocular hemorrhage (OR, 1.68; 95% CI, 0.95-2.98; P = 0.07), monthly versus PRN/0.0 mg for nonocular hemorrhage (OR, 1.54; 95% CI, 0.98-2.42; P = 0.06), monthly versus PRN for ATE (OR, 1.58; 95% CI, 0.96-2.61; P = 0.07), and monthly versus PRN/0.0 mg for ATE (OR, 1.42; 95% CI, 0.99-2.05; P = 0.06). Among the other analyses, no protective or harmful effects of ranibizumab were observed.

CONCLUSION: In ranibizumab treatment for patients with AMD, a possible relationship of more intensive treatment to more systemic vascular adverse events was identified, but no relationship with mortality was identified.

PMID: 25023760 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2014 Jun 24;8:1187-98. doi: 10.2147/OPTH.S40350. eCollection 2014.

Ranibizumab for the treatment of degenerative ocular conditions.

Triantafylla M, Massa HF, Dardabounis D, Gatzioufas Z, Kozobolis V, Ioannakis K, Perente I, Panos GD.

Abstract: Degenerative ocular conditions, such as age-related macular degeneration, diabetic retinopathy, retinal vein occlusions, and myopic degeneration, have become a major public health problem and a leading cause of blindness in developed countries. Anti-vascular endothelial growth factor (VEGF) drugs seem to be an effective and safe treatment for these conditions. Ranibizumab, a humanized monoclonal antibody antigen-binding fragment, which inhibits all biologically active isoforms of VEGF-A, is still the gold standard treatment for the majority of these pathological entities. In this review, we present the results of the most important clinical trials concerning the efficacy and safety of ranibizumab for the treatment of degenerative ocular conditions.

PMID: 25028531 [PubMed] PMCID: PMC4077856

Optom Vis Sci. 2014 Jul 17. [Epub ahead of print]

Photodynamic Therapy for Choroidal Hemangioma Unresponsive to Ranibizumab.

Chan LW, Hsieh YT.

PURPOSE: To report a patient with circumscribed choroidal hemangioma with serous macular detachment successfully treated with photodynamic therapy (PDT) after being unresponsive to treatment with intravitreal ranibizumab.

CASE REPORT: A 63-year-old Asian woman was incidentally found to have a circumscribed choroidal hemangioma without symptoms in the left eye during a routine health examination. Blurred vision of the left eye developed 3.5 years later, and a serous macular detachment was observed. Two consecutive intravitreal ranibizumab injections were administered, but the subretinal fluid (SRF) persisted and the vision did not improve. One PDT session was then given, and the SRF resolved completely within 1 month. The best-corrected visual acuity improved from 20/50 before treatment to 20/25 at 4 months after the PDT. The tumor thickness also decreased from 3.84 mm before treatment to 2.86 mm at 14 months after PDT.

CONCLUSIONS: Circumscribed choroidal hemangioma with serous macular detachment may not respond to anti-vascular endothelial growth factor agents. Photodynamic therapy may be an effective choice in such

cases to remove SRF and improve vision.

PMID: 25036544 [PubMed - as supplied by publisher]

Psychol Health Med. 2014 Jul 18:1-15. [Epub ahead of print]

Experiences of patients undergoing anti-VEGF treatment for neovascular age-related macular degeneration: A systematic review.

Boyle J, Vukicevic M, Koklanis K, Itsiopoulos C.

Abstract: Current therapy to slow disease progression in patients with neovascular age-related macular degeneration (AMD) often entails intra-vitreal injection of an anti-vascular endothelial growth factor (VEGF) agent, that begins with a three-month loading phase of four weekly injections followed by regular monthly visits with clinician-determined re-treatment. The effects of AMD on quality of life and visual function have been extensively reported in the literature, however, less is known about the burden imposed on patients by the arduous and often indefinite treatment schedule which habitually follows a diagnosis of wet AMD. To date, no systematic review has been conducted of research investigating patients' experiences of anti-VEGF treatment for AMD. A systematic search of the Embase, Medline, PsycINFO and PubMed electronic databases was undertaken to identify all studies between January 2004 and December 2013, published in the English language and involving human participants. A hand-search of an additional four journals was conducted. Ten articles were identified for inclusion in this review. A critical appraisal was undertaken using the Critical Appraisal Skills Programme Qualitative Research Checklist and the results synthesised to form a narrative review. Few studies to date have investigated patients' experiences of treatment for AMD. These studies have focused primarily on patients' experiences of the injection procedure with respect to pain and anxiety. Anticipated discomfort is often greater than actual discomfort experienced during intra-vitreal injection. However, different stages of the treatment procedure produce varying levels of patient discomfort. No one method of anaesthesia has consistently been shown to be more effective in reducing discomfort associated with treatment. Common reasons underlying patient apprehension surrounding treatment include the thought of having an injection, fear of losing eyesight and fear of the unknown. Whilst these studies have not been without their methodological limitations, they provide a platform for further exploration of the patient experience.

PMID: 25034616 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Prog Retin Eye Res. 2014 Jul 16. pii: S1350-9462(14)00041-X. doi: 10.1016/j.preteyeres.2014.07.001. [Epub ahead of print]

Cellular responses following retinal injuries and therapeutic approaches for neurodegenerative diseases.

Cuenca N, Fernández-Sánchez L, Campello L, Maneu V, De la Villa P, Lax P, Pinilla I.

Abstract: Retinal neurodegenerative diseases like age-related macular degeneration, glaucoma, diabetic retinopathy and retinitis pigmentosa each have a different etiology and pathogenesis. However, at the cellular and molecular level, the response to retinal injury is similar in all of them, and results in morphological and functional impairment of retinal cells. This retinal degeneration may be triggered by gene defects, increased intraocular pressure, high levels of blood glucose, other types of stress or aging, but they all frequently induce a set of cell signals that lead to well-established and similar morphological and functional changes, including controlled cell death and retinal remodeling. Interestingly, an inflammatory response, oxidative stress and activation of apoptotic pathways are common features in all these diseases.

Furthermore, it is important to note the relevant role of glial cells, including astrocytes, Müller cells and microglia, because their response to injury is decisive for maintaining the health of the retina or its degeneration. Several therapeutic approaches have been developed to preserve retinal function or restore eyesight in pathological conditions. In this context, neuroprotective compounds, gene therapy, cell transplantation or artificial devices should be applied at the appropriate stage of retinal degeneration to obtain successful results. This review provides an overview of the common and distinctive features of retinal neurodegenerative diseases, including the molecular, anatomical and functional changes caused by the cellular response to damage, in order to establish appropriate treatments for these pathologies.

PMID: 25038518 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2014 Jul 17. pii: IOVS-14-14802. doi: 10.1167/iovs.14-14802. [Epub ahead of print]

Quantitative autofluorescence and cell density maps of the human retinal pigment epithelium.

Ach T, Huisingh C, McGwin G, Messinger JD, Zhang T, Bentley MJ, Gutierrez DB, Ablonczy Z, Smith RT, Sloan KR, Curcio CA.

Purpose: Lipofuscin (LF) accumulation within retinal pigment epithelium (RPE) cells is considered pathogenic in age-related macular degeneration (AMD). To test whether LF contributes to RPE cell loss in aging and to provide a cellular basis for fundus autofluorescence (AF) we created maps of human RPE cell number and histological AF.

Methods: RPE-Bruch's membrane flat mounts were prepared from 20 donor eyes (10≤51 and 10>80 years; post-mortem: ≤4.2 hours; no retinal pathologies), preserving foveal position. Phalloidin-binding RPE cytoskeleton and LF-AF (488 nm excitation) were imaged at up to 90 predefined positions. Maps were assembled from 83,336 cells in 1,470 locations. From Voronoi regions representing each cell, the number of neighbors, cell area, and total AF intensity normalized to an AF standard was determined.

Results: Highly variable between individuals, RPE-AF increases significantly with age. A perifoveal ring of high AF mirrors rod photoreceptor topography and fundus-AF. RPE cell density peaks at the fovea, independent of age, yet no net RPE cell loss is detectable. The RPE monolayer undergoes considerable lifelong re-modeling. The relationship of cell size and AF, a surrogate for LF concentration, is orderly and linear in both groups. AF topography differs distinctly from the topography of age-related rod loss.

Conclusions: Digital maps of quantitative AF, cell density, and packing geometry provide metrics for cellular -resolution clinical imaging and model systems. The uncoupling of RPE LF content, cell number, and photoreceptor topography in aging challenges LF's role in AMD.

PMID: 25034602 [PubMed - as supplied by publisher]

Ophthalmologe. 2014 Jul 19. [Epub ahead of print]

[Serous vascularized pigment epithelial detachment in exudative AMD : Morphological typing and risk of tears in the RPE.] [Article in German]

Lehmann B, Heimes B, Gutfleisch M, Spital G, Pauleikhoff D, Lommatzsch A.

PURPOSE: Are there any morphological parameters in pigment epithelial detachment (PED) in eyes with age-related macular degeneration (AMD), which could identify the development of tears (RIP) in the retinal pigment epithelium (RPE) before initiation of anti-vascular endothelial growth factor (VEGF) therapy?

METHODS: Retrospectively, the spectral domain optical coherence tomography (SD-OCT), FLA and near infrared (NIR) images of 98 eyes with PED in exudative AMD before treatment (ranibizumab or

bevacizumab) were analyzed. Eyes in which a tear in the RPE (RIP group) could be observed during treatment were compared to eyes without the development of RIP (PED group) in the following morphological parameters of PED: height, number of peaks, presence of hyporeflective fissures at the base of the PED, structure of the RPE, presence of floating structures in the PED with maximum hyperreflectivity, amount and localization of hyperreflectivity in the PED and hyperreflectivity in the NIR images.

RESULTS: In the 80 eyes of the PED group the mean PED height was 373.7± 197 µm and in the 18 eyes of the RIP group the mean PED height was higher (694.2± 284.3 µm, $p < 0.0001$). A difference was also seen in the number of peaks per PED (PED group 43 %, RIP group 72 %, $p = 0.039$) and in the hyperreflectivity in NIR images (PED group 68 %, RIP group 94 %, $p = 0.033$). There were no significant differences in the other morphological parameters. A classification into four types of PED was found by the parameters height and number of peaks. The PED type with a height > 350 µm and one peak (RIP 43 %) developed tears more often ($p = 0.001$) than the PED type < 350 µm with one peak (RIP 0 %, $p = 0.001$). A trend in the visual acuity over 156 weeks was seen: in PED types with heights > 350 µm there was a lower increase in the visual acuity than in PED types < 350 µm (rm ANOVA $p = 0.18$; ε HH = 0.88). Furthermore, in PED types > 350 µm with multiple peaks the total number of injections necessary was higher than in the other PED types ($p = 0.032$).

CONCLUSION: Morphological parameters, such as PED height, number of peaks per PED in OCT images and hyperreflectivity in NIR images are prognostic factors for RPE tears in exudative AMD. The PED height and number of peaks per PED are useful for classification of PED in the daily routine.

PMID: 25033948 [PubMed - as supplied by publisher]

J Ophthalmol. 2014;2014:459136. doi: 10.1155/2014/459136. Epub 2014 Jun 16.

Examining the choroid in ocular inflammation: a focus on enhanced depth imaging.

Baltmr A, Lightman S, Tomkins-Netzer O.

Abstract: The choroid is the vascular layer that supplies the outer retina and is involved in the pathogenesis of several ocular conditions including choroidal tumors, age related macular degeneration, central serous chorioretinopathy, diabetic retinopathy, and uveitis. Nevertheless, difficulties in the visualization of the choroid have limited our understanding of its exact role in ocular pathology. Enhanced depth imaging optical coherent topography (EDI-OCT) is a novel, noninvasive technique that is used to evaluate choroidal thickness and morphology in these diseases. The technique provides detailed objective in vivo visualization of the choroid and can be used to characterize posterior segment inflammatory disorders, monitor disease activity, and evaluate efficacy of treatment. In this review we summarize the current application of this technique in ocular inflammatory disorders and highlight its utility as an additional tool in monitoring choroidal involvement in ocular inflammation.

PMID: 25024846 [PubMed] PMCID: PMC4082870

Retina. 2014 Jun 25. [Epub ahead of print]

THE PEARL NECKLACE SIGN: A Novel Spectral Domain Optical Coherence Tomography Finding in Exudative Macular Disease.

Gelman SK, Freund KB, Shah VP, Sarraf D.

PURPOSE: To report a novel spectral domain optical coherence tomography finding in exudative macular disease, called the pearl necklace sign.

METHODS: A retrospective case series of 21 eyes (20 patients) with chronic exudative maculopathy

resulting from age-related macular degeneration, diabetic macular edema, branch retinal vein occlusion, retinal arterial macroaneurysm, and Coats disease. Spectral domain optical coherence tomography images were carefully evaluated and correlated with color fundus photography, near-infrared reflectance, and fluorescein angiography.

RESULTS: A unique spectral domain optical coherence tomography macular finding of hyperreflective dots in a contiguous ring around the inner wall of cystoid spaces in the outer plexiform layer of the retina that the authors refer to as the pearl necklace sign was seen in all patients. Visual acuity ranged from 20/30 to hand motions. The cystoid spaces and the hyperreflective dots resolved in certain cases after anti-vascular endothelial growth factor therapy and/or focal macular laser, but tended to recur.

CONCLUSION: Because the pearl necklace configuration can be found adjacent to hard exudates in the outer plexiform layer, the authors speculate that the hyperreflective material is composed of lipoproteins or lipid-laden macrophages. This novel spectral domain optical coherence tomography sign gives further insight into the development and progression of hard lipoprotein exudates in exudative maculopathy.

PMID: 25020214 [PubMed - as supplied by publisher]

Recent Pat Drug Deliv Formul. 2014 Jul 13. [Epub ahead of print]

Patent Perspectives for Corticosteroids Based Ophthalmic Therapeutics.

Suresh PK, Sah AK.

Abstract: Eye inflammation, if untreated at right time poses the risk of vision loss. Several categories of drugs are available in the global market, but corticosteroids are still used for the treatment of ocular inflammation including anterior/posterior uveitis, age related macular degeneration (AMD) and post cataract surgery inflammation. Although corticosteroids have well-documented side effects as compared to non steroidal anti-inflammatory drugs (NSAIDs), but they are still regarded as better anti-inflammatory agents for treating ocular inflammations. The prime concern with conventional formulations such as (ophthalmic solutions, suspensions, ointments) is low drug bioavailability due to precorneal barrier of the eye, tear turnover and rapid drainage of drug via nasolacrimal drainage and drug induced systemic toxicity. To overcome these limitations, various novel formulations of corticosteroids have been explored. These include nanoparticles, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), nanomicelles, in-situ gels, iontophoresis, liposomes, nanoemulsions, microemulsions and ocular implants for the effective ophthalmic delivery of the corticosteroids. Topical nanocarriers have also been demonstrated to be promising vectors with potential application in the ophthalmic therapeutics. This review summarizes the clinical findings and patents on various corticosteroids as ocular pharmacotherapeutics.

PMID: 25020063 [PubMed - as supplied by publisher]

Pathogenesis

Invest Ophthalmol Vis Sci. 2014 Jul 17. pii: IOVS-14-14566. doi: 10.1167/iovs.14-14566. [Epub ahead of print]

Wnt Modulators in the Aqueous Humor are Associated with Outer Retinal Damage Severity in Patients with Neovascular Age-related Macular Degeneration.

Park KH, Choi AJ, Yoon J, Lim D, Woo SJ, Park SJ, Kim HC, Chung H.

Purpose: To investigate the associations of the Wnt modulators Wnt inhibitory factor 1 (WIF-1) and

Dickkopf 3 (DKK-3) in the aqueous humor (AH) with neovascular age-related macular degeneration (nAMD) and to determine their clinical implications.

Methods: Seventy-four nAMD patients initially treated with an intravitreal injection of ranibizumab (IVR) and 74 age- and gender-matched controls were studied. AH WIF-1 and DKK-3 levels were measured by western blotting and an ELISA before and one month after two consecutive IVRs (pre- and post-IVR). Visual acuity assessments and spectral domain optical coherence tomography were performed pre- and post-IVR.

Results: Western blotting showed increased WIF-1 and DKK-3 in 12 nAMD patients compared with 12 controls. ELISA analysis demonstrated elevated WIF-1 (pre) and DKK-3 (pre) in 62 patients compared with 62 controls (54.7 vs. 23.0 and 114.3 vs. 93.0 ng/mL, respectively). In multivariate analyses, high WIF-1 (pre) levels were associated with increased disruption in the photoreceptor junction's inner and outer segments (IS/OS) (pre and post) and high WIF-1 (post) levels. Interestingly, WIF-1 (pre) levels were significantly higher in type 3 neovascularization (NV) patients than in type 1 or 2 NV (90.5±36.7 vs. 48.3±22.5 and 41.3±28.8 ng/mL, respectively). However, choroidal thickness was not correlated with WIF-1 levels.

Conclusions: We report, for the first time, the possibility of phenotypic, anatomic, and ocular proteomic correlations, demonstrating correlated WIF-1 and DKK-3 upregulation in nAMD patients' AH. Secreted WIF-1, reflecting the degree of retinal structure damage, may be a new biomarker for the retina's healthy and disease states.

PMID: 25034605 [PubMed - as supplied by publisher]

Am J Pathol. 2014 Jul 11. pii: S0002-9440(14)00316-2. doi: 10.1016/j.ajpath.2014.06.001. [Epub ahead of print]

Complement Regulatory Protein CD46 Protects against Choroidal Neovascularization in Mice.

Lyzogubov V, Wu X, Jha P, Tytarenko R, Triebwasser M, Kolar G, Bertram P, Bora PS, Atkinson JP, Bora NS.

Abstract: Dysregulation of the complement system is increasingly recognized as a contributing factor in age -related macular degeneration. Although the complement regulator CD46 is expressed ubiquitously in humans, in mouse it was previously thought to be expressed only on spermatozoa. We detected CD46 mRNA and protein in the posterior ocular segment (neuronal retina, retinal pigment epithelium, and choroid) of wild-type (WT) C57BL/6J mice. Cd46-/- knockout mice exhibited increased levels of the membrane attack complex and of vascular endothelial growth factor (VEGF) in the retina and choroid. The Cd46-/- mice were also more susceptible to laser-induced choroidal neovascularization (CNV). In Cd46-/- mice, 19% of laser spots were positive for CNV at day 2 after treatment, but no positive spots were detected in WT mice. At day 3, 42% of laser spots were positive in Cd46-/- mice, but only 11% in WT mice. A fully developed CNV complex was noted in both Cd46-/- and WT mice at day 7; however, lesion size was significantly ($P < 0.05$) increased in Cd46-/- mice. Our findings provide evidence for expression of CD46 in the mouse eye and a role for CD46 in protection against laser-induced CNV. We propose that the Cd46-/- mouse has a greater susceptibility to experimental CNV because of insufficient complement inhibition, which leads to increased membrane attack complex deposition and VEGF expression.

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The influence of substrate elastic modulus on retinal pigment epithelial cell phagocytosis.

Boochoon KS, Manarang JC, Davis JT, McDermott AM, Foster WJ.

Abstract: To better understand if a complex process such as phagocytosis is influenced by substrate stiffness, we investigated the influence of substrate elastic modulus on phagocytosis in the retinal pigment epithelial (RPE) cell line ARPE-19. RPE cells lie on Bruch′s membrane, directly under the retina, and phagocytose the shed photoreceptor outer segments. Bruch′s membrane is known to increase in stiffness by an order of magnitude with age and thus, this study has potential relevance in explaining retinal changes in age-related macular degeneration. ARPE-19 cells were plated on laminin-coated polyacrylamide substrates of varying elastic modulus. After 14 days in culture, a solution of latex fluorescent beads suspended in PBS was placed in each well. After an incubation time of 4h, flow cytometry was performed to determine the number of cells that phagocytosed a bead. The number of ARPE-19 cells that phagocytosed a bead decreased continuously as a function of increasing substrate elastic modulus (p=0.0135), and this was found to be a linear relationship (slope=-0.03305±0.01104, R2=0.4726 per 10,000 cells). Our results suggest that RPE cells display decreased phagocytosis when grown on firmer substrates, and thus, RPE cells in older eyes, in which Bruch′s membrane is stiffer, may demonstrate decreased phagocytosis. Impaired phagocytosis by RPE cells may contribute to impaired metabolism of photoreceptor outer segments and to development of macular degeneration. Material stiffness may be a critical parameter in the development of neural therapies, including retinal prosthetics and stem cell therapies.

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7-Ketocholesterol-Induced Inflammation Signals Mostly through the TLR4 Receptor Both In Vitro and In Vivo.

Huang JD, Amaral J, Lee JW, Rodriguez IR.

Abstract: The cholesterol oxide 7-ketocholesterol (7KCh) has been implicated in numerous age-related diseases such as atherosclerosis, Alzheimer's disease, Parkinson's disease, cancer and age-related macular degeneration. It is formed by the autooxidation of cholesterol and especially cholesterol-fatty acid esters found in lipoprotein deposits. This molecule causes complex and potent inflammatory responses in vitro and in vivo. It is suspected of causing chronic inflammation in tissues exposed to oxidized lipoprotein deposits. In this study we have examined the inflammatory pathways activated by 7KCh both in cultured ARPE19 cells and in vivo using 7KCh-containing implants inserted into the anterior chamber of the rat eye. Our results indicate that 7KCh-induced inflammation is mediated mostly though the TLR4 receptor with some cross-activation of EGFR-related pathways. The majority of the cytokine inductions seem to signal via the TRIF/TRAM side of the TLR4 receptor. The MyD88/TIRAP side only significantly effects IL-1β inductions. The 7KCh-induced inflammation also seems to involve a robust ER stress response. However, this response does not seem to involve a calcium efflux-mediated UPR. Instead the ER stress response seems to be mediated by yet identified kinases activated through the TLR4 receptor. Some of the kinases identified are the RSKs which seem to mediate the cytokine inductions and the cell death pathway but do not seem to be involved in the ER stress response.

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Epidemiology

Am J Ophthalmol. 2014 Jul 14. pii: S0002-9394(14)00397-3. doi: 10.1016/j.ajo.2014.07.006. [Epub ahead of print]

The Incidence of Neovascular Subtypes in Newly Diagnosed Neovascular Age-Related Macular Degeneration.

Jung JJ, Chen CY, Mrejen S, Gallego-Pinazo R, Xu L, Marsiglia M, Boddu S, Freund KB.

PURPOSE: To determine the frequency of neovascularization subtypes as determined by fluorescein angiography (FA) alone versus FA and optical coherence tomography (OCT) grading in age-related macular degeneration (AMD).

DESIGN: Retrospective cohort METHODS: Participants: Newly diagnosed neovascular AMD patients who initiated intravitreal anti-vascular endothelial growth factor therapy by one physician from October 1st, 2005 to December 1st, 2012.

INTERVENTIONS: Two independent graders classified the baseline lesions using FA alone and FA+OCT.

MAIN OUTCOME MEASURES: Analysis of the frequency of lesion subtypes by FA alone or FA+OCT and agreement between both classification systems was performed.

RESULTS: 232 patients (266 eyes) fit the inclusion criteria. Mean age was 86.3 years; 67.7%(180/266) were women, and 95.5%(254/266) were Caucasian. The distribution using FA alone was 49.6%(132/266), 12.0%(32/266), 28.6%(76/266) and 9.8%(26/266) among occult, classic, retinal angiomatous proliferation and mixed choroidal neovascularization, respectively. With FA+OCT, 39.9%(106/266), 9.0%(24/266), 34.2%(91/266), and 16.9%(45/266) were type 1 (sub-retinal pigment epithelium), type 2 (sub-retinal), type 3 (intra-retinal), and mixed neovascularization (NV), respectively. The κ statistic was 0.65 (standard error ±0.37, p<0.001) between the two classification systems representing good agreement.

CONCLUSION: With both FA alone and FA+OCT grading, we found a higher incidence of type 3 NV in eyes with newly diagnosed neovascular AMD than that reported in prior studies. The κ statistic between the two classification systems showed "good" agreement. The discrepancies are likely due to the identification of a higher frequency of Type 3 and mixed NV and a lower frequency of type 1 NV with the aid of OCT.

PMID: 25034111 [PubMed - as supplied by publisher]

J Alzheimers Dis. 2014 Jul 2. [Epub ahead of print]

Macular Pigment, Visual Function, and Macular Disease among Subjects with Alzheimer's Disease: An Exploratory Study.

Nolan JM, Loskutova E, Howard AN, Moran R, Mulcahy R, Stack J, Bolger M, Dennison J, Akuffo KO, Owens N, Thurnham DI, Beatty S.

Background: The macula (central retina) contains a yellow pigment, comprising the dietary carotenoids lutein (L), zeaxanthin (Z), and meso-zeaxanthin, known as macular pigment (MP). The concentrations of MP's constituent carotenoids in retina and brain tissue correlate, and there is a biologically-plausible rationale, supported by emerging evidence, that MP's constituent carotenoids are also important for cognitive function. Objective: To investigate if patients with Alzheimer's disease (AD) are comparable to controls in terms of MP and visual function.

Methods: 36 patients with moderate AD and 33 controls with the same age range participated. MP was measured using dual-wavelength autofluorescence (Heidelberg Spectralis®); cognitive function was assessed using a battery of cognition tests (including Cambridge Neuropsychological Test Automated Battery). Visual function was recorded by measuring best corrected visual acuity (BCVA) and contrast sensitivity (CS). Serum L and Z concentrations (by HPLC) and age-related macular degeneration (AMD, by retinal examination) status were also assessed.

Results: In the AD group, central MP (i.e., at 0.23°) and MP volume were significantly lower than the control group ($p < 0.001$ for both), as were measures of BCVA, CS, and serum L and Z concentrations ($p < 0.05$, for all).

Conclusion: AD patients were observed to exhibit significantly less MP, lower serum concentrations of L and Z, poorer vision, and a higher occurrence of AMD when compared to control subjects. A clinical trial in AD patients designed to investigate the impact of macular carotenoid supplementation with respect to MP, visual function, and cognitive function is merited.

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J Alzheimers Dis. 2014 Jul 2. [Epub ahead of print]

The Prevalence of Age-Related Macular Degeneration in Alzheimer's Disease.

Williams MA, Silvestri V, Craig D, Passmore AP, Silvestri G.

Background: Age-related macular degeneration (AMD) and Alzheimer's disease (AD) share several features, including the presence of extracellular abnormal deposits associated with neuronal degeneration, drusen, and plaques, respectively. Investigation of any association of AMD and specifically AD is worthwhile but has rarely been done. Objectives: The aim of this study was to determine the prevalence of AMD in subjects with AD in comparison with an age-matched cognitively normal cohort.

Methods: Cases were defined as those diagnosed with AD using standardized criteria as part of their clinical care, while controls were cognitively intact individuals aged 65 years or more. Dilated retinal photographs were taken, and a range of potentially confounding factors measured including APOE genotype. AMD features were recorded and AMD grades given.

Results: Data was collected on 322 controls and 258 cases. While AMD was associated with AD, and the proportion of cases of advanced AMD in AD cases was twice that of controls, when corrected the association was lost. AD was associated with age, the presence of an APOE allele, and smoking, while being 'generally unwell recently' was associated with a reduced risk of AD.

Conclusion: AD and AMD are both associated with age, but our study does not find evidence they are associated with each other. However the retina offers an opportunity to non-invasively image neuronal tissue, and more sophisticated imaging techniques may shed light on ocular biomarkers of AD.

PMID: 25024309 [PubMed - as supplied by publisher]

PLoS One. 2014 Jul 15;9(7):e102816. doi: 10.1371/journal.pone.0102816. eCollection 2014.

Association between Reproductive Factors and Age-Related Macular Degeneration in Postmenopausal Women: The Korea National Health and Nutrition Examination Survey 2010-2012.

Cho BJ, Heo JW, Shin JP, Ahn J, Kim TW, Chung H.

PURPOSE: To examine the association between female reproductive factors and age-related macular degeneration (AMD) in postmenopausal women.

DESIGN: Nationwide population-based cross-sectional study.

METHODS: A nationally representative dataset acquired from the 2010-2012 Korea National Health and Nutrition Examination Survey was analyzed. The dataset involved information for 4,377 postmenopausal women aged ≥50 years with a fundus photograph evaluable for AMD in either eye. All participants were interviewed using standardized questionnaires to determine reproductive factors including menstruation, pregnancy, parity, lactation, and hormonal use. The association between reproductive factors and each type of AMD was investigated.

RESULTS: The mean age of the study participants was 63.1±0.2 years. Mean ages at menarche and

menopause were 16.1±0.0 and 49.2±0.1 years, respectively. The overall prevalence rates of early and late AMD were 11.2% (95% confidence interval [CI], 10.1-12.5) and 0.8% (95% CI, 0.5-1.2), respectively. When adjusted for age, neither smoking nor alcohol use was associated with the presence of any AMD or late AMD. Multivariate logistic regression analysis revealed age (OR, 1.12 per 1 year), duration of lactation (OR, 0.91 per 6 months), and duration of use of oral contraceptive pills (OCP) (OR, 1.10 per 6 months) as associated factors for late AMD. The other variables did not yield a significant correlation with the risk of any AMD or late AMD.

CONCLUSION: After controlling for confounders, a longer duration of lactation appeared to protect against the development of late AMD. A longer duration of OCP use was associated with a higher risk of late AMD.

PMID: 25025761 [PubMed - in process]

Nihon Ganka Gakkai Zasshi. 2014 Jun;118(6):495-501.

[Causes and prevalence of visual impairment in Japan].[Article in Japanese]

Wako R, Yasukawa T, Kato A, Omori T, Ishida S, Ishibashi T, Ogura Y.

PURPOSE: To investigate the causes of visual impairment in Japan.

METHODS: The documents of 4,852 individuals with authorization of visual impairment registered between April 2007 and March 2010 in 7 randomly selected regions were reviewed.

RESULTS: The major causes of visual impairment were glaucoma (21.0%), diabetic retinopathy (15.6%), retinitis pigmentosa (12.0%), macular degeneration (9.5%) and chorioretinal atrophy (8.4%). Individuals over 70 years of age were predominant for glaucoma, those aged 50-69 years for diabetic retinopathy and those under 40 years of age for retinitis pigmentosa. Sixty-one percent of persons affected by glaucoma were severely handicapped. Macular degeneration increased with age especially in individuals over 80 years of age.

CONCLUSION: There was no difference in the order of major causes as compared with a previous report in 2001-2004. It is important to establish a central database system so that the data can be surveyed to provide more relevant information to understand current issues for handicapped persons and develop new prophylactic and therapeutic modalities.

PMID: 25016791 [PubMed - in process]

Genetics

Hum Hered. 2014 Jul 12;78(2):59-72. [Epub ahead of print]

(Epi)Genetic Analyses of Age-Related Macular Degeneration: Case-Control and Discordant Twin Studies.

Hutchinson JN, Fagerness J, Kirby A, Reynolds R, Zak A, Gimelbrant A, Plenge R, Daly M, Chess A, Seddon JM.

Background/Aims: Phenotypic discordance in monozygotic (MZ) twin pairs can have an epigenetic or genetic basis. Although age-related macular degeneration (AMD) has a strong genetic component, few studies have addressed its epigenetic basis.

Methods: Using SNP arrays, we evaluated differences in copy number variation (CNV) and allele-specific methylation (ASM) patterns (via methyl-sensitive restriction enzyme digestion of DNA) in MZ twin pairs from the US Twin Study of AMD. Further analyses examined the relationship between ASM and CNVs with AMD

by both case/control analysis of ASM at candidate regions and by analysis of ASM and CNVs in twins discordant for AMD.

Results: The frequency of ASM sites differs between cases and controls in regions surrounding the AMD candidate genes CFH, C2 and CFB. While ASM patterns show a substantial dependence on local sequence polymorphisms, we observed dissimilar patterns of ASM between MZ twins. The genes closest to the sites where discordant MZ twins have dissimilar patterns of ASM are enriched for genes implicated in gliosis, a process associated with neovascular AMD. Similar twin-based analyses revealed no AMD-associated CNVs.

Conclusions: Our results provide evidence of epigenetic influences beyond the known genetic susceptibility and implicate inflammatory responses and gliosis in the etiology of AMD.

PMID: 25033836 [PubMed - as supplied by publisher]

Genes (Basel). 2014 Jul 16;5(3):518-35. doi: 10.3390/genes5030518.

The impact of the human genome project on complex disease.

Bailey JN, Pericak-Vance MA, Haines JL.

Abstract: In the decade that has passed since the initial release of the Human Genome, numerous advancements in science and technology within and beyond genetics and genomics have been encouraged and enhanced by the availability of this vast and remarkable data resource. Progress in understanding three common, complex diseases: age-related macular degeneration (AMD), Alzheimer's disease (AD), and multiple sclerosis (MS), are three exemplars of the incredible impact on the elucidation of the genetic architecture of disease. The approaches used in these diseases have been successfully applied to numerous other complex diseases. For example, the heritability of AMD was confirmed upon the release of the first genome-wide association study (GWAS) along with confirmatory reports that supported the findings of that state-of-the art method, thus setting the foundation for future GWAS in other heritable diseases. Following this seminal discovery and applying it to other diseases including AD and MS, the genetic knowledge of AD expanded far beyond the well-known APOE locus and now includes more than 20 loci. MS genetics saw a similar increase beyond the HLA loci and now has more than 100 known risk loci. Ongoing and future efforts will seek to define the remaining heritability of these diseases; the next decade could very well hold the key to attaining this goal.

PMID: 25032678 [PubMed]

Inflammation. 2014 Jul 16. [Epub ahead of print]

Genetic Variants of Interleukin 17A Are Functionally Associated with Increased Risk of Age-Related Macular Degeneration.

Zhang S, Liu Y, Lu S, Cai X.

Abstract: Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in elderly populations worldwide. Inflammation, among many factors, has been suggested to play an important role in AMD pathogenesis. Interleukin 17 (IL-17) is a proinflammatory cytokine that has been implicated in the pathogenesis of various autoimmune diseases. In the current study, we examined two single nucleotide polymorphisms (SNPs), rs2275913G/A and rs3748067C/T, in the IL-17A gene between AMD patients and healthy controls. Results showed that rs2275913AA genotype and rs3748067TT genotype were associated with increased susceptibility to AMD (hazard ratio [HR], 1.75; 95 % confidence interval [CI], 1.07 to 3.02; P = 0.023, and HR, 2.12; 95 % CI, 1.26 to 4.01; P = 0.004; data were adjusted for age and sex). Next, we investigated the functional relevance of the two SNPs. In vitro stimulated peripheral blood mononuclear

cells (PBMCs) from subjects possessing the rs2275913AA genotype produced significantly more IL-17 than those with the GG genotype. However, PBMCs with rs3748067TT genotype revealed significantly higher IL-17 production than those with rs3748067CC genotype only in AMD patients but not in controls. These data indicate IL-17A polymorphisms are associated with increased risk of AMD probably by affecting gene expression.

PMID: 25028103 [PubMed - as supplied by publisher]

Mol Immunol. 2014 Jul 15. pii: S0161-5890(14)00163-1. doi: 10.1016/j.molimm.2014.06.032. [Epub ahead of print]

Genetic variants in the complement system predisposing to age-related macular degeneration: A review.

Schramm EC, Clark SJ, Triebwasser MP, Raychaudhuri S, Seddon JM, Atkinson JP.

Abstract: Age-related macular degeneration (AMD) is a major cause of visual impairment in the western world. It is characterized by the presence of lipoproteinaceous deposits (drusen) in the inner layers of the retina. Immunohistochemistry studies identified deposition of complement proteins in the drusen as well as in the choroid. In the last decade, genetic studies have linked both common and rare variants in proteins of the complement system to increased risk of development of AMD. Here, we review the variants described to date and discuss the functional implications of dysregulation of the alternative pathway of complement in AMD.

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Diet & lifestyle

Int J Food Sci Nutr. 2014 Jul 14:1-7. [Epub ahead of print]

Bioavailability of lutein from a lutein-enriched egg-yolk beverage and its dried re-suspended versions.

Bunger M, Quataert M, Kamps L, Versloot P, Hulshof PJ, Togtema A, van Amerongen A, Mensink M.

Abstract: Drying a fresh lutein-enriched egg-yolk beverage would extend its shelf life, however, functional properties should not be affected. It was investigated whether consumption of a dried beverage containing lutein-enriched egg-yolk significantly increases serum lutein. One-hundred healthy young subjects participated in this 6-weeks randomized controlled study. Subjects consumed either a "plain" control beverage (n = 26), a fresh lutein-enriched egg-yolk beverage (n = 25), a dried version of this beverage (n = 25), or a beverage composed of the dried individual components of the drink (n = 24). The fresh and both dried versions of the lutein-enriched egg-yolk beverage were able to increase serum lutein levels after 6 weeks of consumption (lutein change: -38 ± 47 nmol/L, +304 ± 113 nmol/L, +148 ± 79 nmol/L and +178 ± 83 nmol/L for control, fresh, dried and combined dried group respectively; $p < 0.001$). No significant change in serum cholesterol level was seen in the beverages containing lutein-enriched egg-yolk compared to the control drink.

PMID: 25017577 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2014 Jul 15. pii: IOVS-14-13918. doi: 10.1167/iovs.14-13918. [Epub ahead of print]

Vitamin D and macular thickness in the elderly: an Optical Coherence Tomography study.

Graffe A, Beauchet O, Fantino B, Milea D, Annweiler C.

Purpose: Vitamin D insufficiency is associated with age-related macular degeneration. Our objective was to determine whether low serum 25-hydroxyvitamin D (25OHD) concentration was associated with macular thickness among older adults with no signs of macular dysfunction.

Methods: Sixty-two French older community-dwellers with no patent macular dysfunction (mean±standard deviation, 71.2±5.0years; 45.2% female) included in the GAIT study (ClinicalTrials.gov number, NCT01315717) were separated into 2 groups according to serum 25OHD level (i.e., insufficient<50nmol/L or sufficient≥50nmol/L). The macular thickness was measured on 1000μm central macula with optical coherence tomography, and further binarized according to normal values of macular thickness (i.e., 267.74μm for males, and 255.60μm for females). Age, gender, number of comorbidities, cognitive disorders, body mass index, mean arterial pressure, visual acuity, intraocular pressure, serum calcium concentration and season of testing were considered as potential confounders.

Results: The mean serum 25OHD concentration was 61.2±26.3nmol/L. Patients with vitamin D insufficiency had a reduced macular thickness compared to those without (232.9±40.4μm versus 253.3±32.1 μm, P=0.042). After adjustment for potential confounders, vitamin D insufficiency was associated with a decreased macular thickness (ß=-59.4μm, P=0.001). Consistently, the participants with vitamin D insufficiency had a 3.7-fold higher risk of having abnormally low macular thickness compared to those with sufficient 25OHD level (P=0.042).

Conclusions: Vitamin D insufficiency was associated with reduced macular thickness among older patients with no patent macular dysfunction. This implies that vitamin D insufficiency may be involved in macular thinning, and provides a scientific base for vitamin D replacement trials in age-related macular degeneration.

PMID: 25028353 [PubMed - as supplied by publisher]

Ophthalmology. 2014 Jun 25. pii: S0161-6420(14)00422-9. doi: 10.1016/j.ophtha.2014.05.002. [Epub ahead of print]

Low Vision Depression Prevention Trial in Age-Related Macular Degeneration: A Randomized Clinical Trial.

Rovner BW, Casten RJ, Hegel MT, Massof RW, Leiby BE, Ho AC, Tasman WS.

PURPOSE: To compare the efficacy of behavior activation (BA) + low vision rehabilitation (LVR) with supportive therapy (ST) + LVR to prevent depressive disorders in patients with age-related macular degeneration (AMD).

DESIGN: Single-masked, attention-controlled, randomized, clinical trial with outcome assessment at 4 months.

PARTICIPANTS: Patients with AMD and subsyndromal depressive symptoms attending retina practices (n = 188).

INTERVENTIONS: Before randomization, all subjects had 2 outpatient LVR visits, and were then randomized to in-home BA+LVR or ST+LVR. Behavior activation is a structured behavioral treatment that aims to increase adaptive behaviors and achieve valued goals. Supportive therapy is a nondirective, psychological treatment that provides emotional support and controls for attention.

MAIN OUTCOME MEASURES: The Diagnostic and Statistical Manual IV defined depressive disorder based on the Patient Health Questionnaire-9 (primary outcome), Activities Inventory, National Eye Institute Vision Function Questionnaire-25 plus Supplement (NEI-VFQ), and NEI-VFQ quality of life (secondary outcomes).

RESULTS: At 4 months, 11 BA+LVR subjects (12.6%) and 18 ST+LVR subjects (23.4%) developed a depressive disorder (relative risk [RR], 0.54; 95% CI, 0.27-1.06; P = 0.067). In planned adjusted analyses the RR was 0.51 (95% CI, 0.27-0.98; P = 0.04). A mediational analysis suggested that BA+LVR prevented depression to the extent that it enabled subjects to remain socially engaged. In addition, BA+LVR was associated with greater improvements in functional vision than ST+LVR, although there was no significant between-group difference. There was no significant change or between-group difference in quality of life.

CONCLUSIONS: An integrated mental health and low vision intervention halved the incidence of depressive disorders relative to standard outpatient LVR in patients with AMD. As the population ages, the number of persons with AMD and the adverse effects of comorbid depression will increase. Promoting interactions between ophthalmology, optometry, rehabilitation, psychiatry, and behavioral psychology may prevent depression in this population.

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