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Drug treatment

Br J Ophthalmol. 2016 Jan 11. [Epub ahead of print]

Changing from a pro re nata treatment regimen to a treat and extend regimen with ranibizumab in neovascular age-related macular degeneration.

Hatz K, Prünte C.

BACKGROUND: Treat and extend (TE) treatment regimens have the potential to reduce the treatment burden placed upon patients receiving ranibizumab for neovascular age-related macular degeneration (nAMD). This study aimed to analyse changes in best corrected visual acuity (BCVA) and anatomical parameters in patients switching from a pro re nata (PRN) to a TE regimen during routine clinical practice.

METHODS: Retrospective, consecutive, comparative case series of treatment-naïve patients who were initially treated with 0.5 mg ranibizumab according to a PRN schedule, and subsequently switched to a TE schedule (12-month follow-up).

RESULTS: 146 eyes from 134 consecutive treatment-naïve patients were included. Mean BCVA (decimal±SD) increased from 0.39±0.23 to 0.55±0.22 ($p<0.001$) during the PRN loading regimen, declining to 0.49±0.22 ($p<0.001$) during the PRN maintenance phase (mean duration 17 months; range 3-55). Following the switch to TE, BCVA improved to 0.55±0.23 and 0.56±0.24 by 6 and 12 months, respectively ($p<0.001$). Mean intraindividual variance in BCVA was higher during the PRN phase than at 12 months for TE (0.30±0.18 vs 0.09±0.08, respectively; $p<0.001$). After switching to TE, mean central retinal thickness decreased from 355±112 µm to 330±105 and 320±103 µm at 6 and 12 months, respectively ($p<0.001$). Mean number of visits per month was higher during PRN than TE periods (1.05±0.13 vs 0.73±0.18; respectively; $p<0.001$).

CONCLUSIONS: A TE regimen can improve and stabilise patient outcomes in nAMD compared with PRN, with the potential to reduce the healthcare resource burden incurred from fixed monitoring requirements.

PMID: 26755642 [PubMed - as supplied by publisher]

J Ophthalmic Inflamm Infect. 2016 Dec;6(1):2. Epub 2016 Jan 12.

Endophthalmitis following intravitreal injection of anti-VEGF agents: long-term outcomes and the identification of unusual micro-organisms.

Sachdeva MM, Moshiri A, Leder HA, Scott AW.

BACKGROUND: While the development of targeted molecular therapy to inhibit vascular endothelial growth factor (VEGF) has revolutionized the treatment and visual prognosis of highly prevalent retinal diseases such as diabetic retinopathy and age-related macular degeneration, each intravitreal injection of these agents carries a small risk of endophthalmitis which can be visually devastating. In the absence of specific

guidelines, current management of post-injection endophthalmitis is typically extrapolated from data regarding endophthalmitis occurring after cataract surgery despite potential differences in pathogenic organisms and clinical course. Here, we assess the contribution of intravitreal injections of anti-VEGF agents to all cases of endophthalmitis at our tertiary care referral center and characterize the clinical outcomes and microbial pathogens associated with post-injection endophthalmitis in order to inform management of this serious iatrogenic condition.

RESULTS: During the 7-year study period analyzed, 199 cases of endophthalmitis were identified using billing records. Of these, the most common etiology was post-surgical, accounting for 62 cases (31.2 %), with bleb-associated, endogenous, and corneal ulcer-related infections representing the next most frequent causes, comprising 15.6 % (31/199), 13.1 % (26/199), and 13.6 % (27/199) of all cases, respectively. Intravitreal injections of anti-VEGF agents represented 8.5 % of endophthalmitis (17/199 cases). Intraocular cultures yielded positive results in 75 % of post-injection cases, with the majority associated with coagulase -negative *Staphylococcus*. Consistent with prior literature, a case of *Strep viridans* displayed more rapid onset and progression. We also report the first association of *Enterobacter cloacae* and *Lactococcus garvieae* with post-injection endophthalmitis. While all but one patient were treated with initial vitreous tap and intravitreal injection of antibiotics, both patients with these rare organisms exhibited persistent vitritis requiring subsequent vitrectomy. Long-term outcomes of post-injection endophthalmitis indicated visual recovery to baseline levels, even with resumption of anti-VEGF agents following resolution of the acute infection.

CONCLUSIONS: Acute endophthalmitis following intravitreal injections of anti-VEGF agents is an uncommon but potentially devastating complication which may be managed effectively with vitreous tap and injection of intravitreal antibiotics. However, persistent vitritis requiring subsequent vitrectomy should raise suspicion for unusual pathogens.

PMID: 26758203 [PubMed]

Other treatment & diagnostics

Doc Ophthalmol. 2016 Jan 11. [Epub ahead of print]

Photoreceptor dysfunction in early and intermediate age-related macular degeneration assessed with mfERG and spectral domain OCT.

Yang S, Zuo C, Xiao H, Mi L, Luo G, Xu X, Liu X.

PURPOSE: To evaluate the changes of the photoreceptor layer (PRL) thickness with spectral domain optical coherence tomography (SD-OCT) and the retinal function by mfERG, as well as the correlation of morphology and function parameters in subjects with early and intermediate age-related macular degeneration (AMD).

METHODS: Subjects with clinical diagnosis of early or intermediate AMD and age-matched healthy subjects were recruited prospectively in this study. Color fundus photography, SD-OCT, and mfERG were conducted. Retinal photoreceptor thickness was measured, and first-order kernel responses were recorded. The differences between AMD group and control group were compared, and the correlations between macular photoreceptor thickness and the mfERG were analyzed.

RESULTS: PRL thickness (μm) in four areas including foveola and 0.5, 1.5, and 3 mm away from foveola was 192.48 ± 17.37 , 163.73 ± 12.95 , 130.93 ± 9.20 , and 108.78 ± 7.81 , respectively, in normal eyes, whereas in AMD group, they were 158.61 ± 45.25 , 138.91 ± 20.92 , 118.91 ± 12.85 , and 95.00 ± 9.64 , respectively ($P < 0.001$). The mean amplitude response densities of AMD patients decreased significantly compared to the control group in ring 1-6 ($P < 0.001$). The mean mfERG N1 and P1 latency of AMD patients prolonged compared to the control group, except the ring 1 ($P = 0.588$ and $P = 0.084$). The macular PRL thickness was significantly associated with the mfERGN1 and P1 amplitude density in ring 1-4 ($r = 0.338$ - 0.533 , $P < 0.01$).

CONCLUSIONS: PRL thickness decreases are in accordance with the deterioration of retinal electrophysiological activity. The retinal PRL thickness is important parameter to assess of early and intermediate AMD severity.

PMID: 26754967 [PubMed - as supplied by publisher]

Pathogenesis

Redox Biol. 2015 Dec 19;8:98-109. [Epub ahead of print]

The novel triterpenoid RTA 408 protects human retinal pigment epithelial cells against H₂O₂-induced cell injury via NF-E2-related factor 2 (Nrf2) activation.

Liu X, Ward K, Xavier C, Jann J, Clark AF, Pang IH, Wu H.

Abstract: Oxidative stress-induced retinal pigment epithelial (RPE) cell damage is an important factor in the pathogenesis of age-related macular degeneration (AMD). Previous studies have shown that RTA 408, a synthetic triterpenoid compound, potently activates Nrf2. This study aimed to investigate the protective effects of RTA 408 in cultured RPE cells during oxidative stress and to determine the effects of RTA 408 on Nrf2 and its downstream target genes. Primary human RPE cells were pretreated with RTA 408 and then incubated in 200µM H₂O₂ for 6h. Cell viability was measured with the WST-8 assay. Apoptosis was quantitatively measured by annexin V/propidium iodide (PI) double staining and Hoechst 33342 fluorescent staining. Reduced (GSH) and oxidized glutathione (GSSG) were measured using colorimetric assays. Nrf2 activation and its downstream effects on phase II enzymes were examined by Western blot. Treatment of RPE cells with nanomolar ranges (10 and 100nM) of RTA 408 markedly attenuated H₂O₂-induced viability loss and apoptosis. RTA 408 pretreatment significantly protected cells from oxidative stress-induced GSH loss, GSSG formation and decreased ROS production. RTA 408 activated Nrf2 and increased the expression of its downstream genes, such as HO-1, NQO1, SOD2, catalase, Grx1, and Trx1. Consequently, the enzyme activities of NQO1, Grx1, and Trx1 were fully protected by RTA 408 pretreatment under oxidative stress. Moreover, knockdown of Nrf2 by siRNA significantly reduced the cytoprotective effects of RTA 408. In conclusion, our data suggest that RTA 408 protect primary human RPE cells from oxidative stress-induced damage by activating Nrf2 and its downstream genes.

PMID: 26773873 [PubMed - as supplied by publisher]

Prog Retin Eye Res. 2016 Jan 7. [Epub ahead of print]

PRPH2/RDS and ROM-1: historical context, current views and future considerations.

Stuck MW, Conley SM, Naash MI.

Abstract: Peripherin2 (PRPH2), also known as RDS (retinal degeneration slow) is a photoreceptor specific glycoprotein which is essential for normal photoreceptor health and vision. PRPH2/RDS is necessary for the proper formation of both rod and cone photoreceptor outer segments, the organelle specialized for visual transduction. When PRPH2/RDS is defective or absent, outer segments become disorganized or fail to form entirely and the photoreceptors subsequently degenerate. Multiple PRPH2/RDS disease-causing mutations have been found in humans, and they are associated with various blinding diseases of the retina such as macular degeneration and retinitis pigmentosa, the vast majority of which are inherited dominantly, though recessive LCA and digenic RP have also been associated with RDS mutations. Since its initial discovery, the scientific community has dedicated a considerable amount of effort to understanding the molecular function and disease mechanisms of PRPH2/RDS. This work has led to an understanding of how the PRPH2/RDS molecule assembles into complexes and functions as a necessary part of the machinery that forms new outer segment discs, as well as leading to fundamental discoveries about the mechanisms that underlie OS biogenesis. Here we discuss PRPH2/RDS-associated research and how experimental results have driven the understanding of the PRPH2/RDS protein and its role in human disease.

PMID: 26773759 [PubMed - as supplied by publisher]

Adv Clin Exp Med. 2015 Nov-Dec;24(6):1099-1104.

The Dry Form of Age-Related Macular Degeneration (AMD): The Current Concepts of Pathogenesis and Prospects for Treatment.

Zajac-Pytrus HM, Pilecka A, Turno-Kręcicka A, Adamiec-Mroczek J, Misiuk-Hojło M.

Abstract: Age-related macular degeneration (AMD) is a disease that causes varying degrees of blindness, which afflicts millions of adults in their later years. Preliminary changes occur during normal aging, but in some individuals the pathology leads to the development of AMD. The pathology seems to be a mixture of biochemical, cellular, and molecular events. Lipofuscinogenesis and early drusen genesis are in the early stages of AMD and their inhibition or reversal would dramatically increase the quality of vision in elderly people. The disease is characterized by abnormal extracellular deposits, known as drusen, which accumulate along the basal surface of the retinal pigmented epithelium RPE. Widespread drusen deposition is associated with retinal pigmented epithelial cell dysfunction and degeneration of the photoreceptors. Recent studies have shown that drusen contain a variety of immunomodulatory molecules, suggesting that the process of drusen formation involves local inflammatory events, including activation of the complement cascade. Molecular pathways involved in the etiology of this disease and the potential prospects of its treatment will be presented on the basis of the results of the current studies.

PMID: 26771984 [PubMed - as supplied by publisher]

Exp Eye Res. 2016 Jan 6;146:107-117. [Epub ahead of print]

Proteomics of vitreous in neovascular age-related macular degeneration.

Nobl M, Reich M, Dacheva I, Siwy J, Mullen W, Schanstra JP, Choi CY, Kopitz J, Kretz FT, Auffarth GU, Koch F, Koss MJ.

Abstract: Neovascular age-related macular degeneration (nAMD) has been described as a predominantly inflammatory and proangiogenic retino-choroidal disease. Vitreous humor (VH) is the adjacent and accessible compartment which, due to the vicinity to the retina, might best represent changes of protein-based mediators of nAMD. The aim of this clinical-experimental study was to analyze the nAMD associated VH proteome of previously untreated patients whilst taking different groups of nAMD into account, based on their clinical presentation (clinical diagnosis groups). Electrophoresis coupled online to mass spectrometry (CE-MS) as well as liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) were used to analyze VH of 108 nAMD patients and 24 controls with idiopathic floaters. A total of 101 different proteins with at least two unique peptides could be identified. Using a stringent statistical analysis with implementation of the closed test principle, we were able to identify four proteins that may be involved in the pathophysiology of nAMD: Clusterin, opticin, pigment epithelium-derived factor and prostaglandin-H2 d-isomerase. Using independent samples, ROC-Area under the curve was determined proving the validity of the results: Clusterin 0.747, opticin 0.656, pigment epithelium-derived factor 0.514, prostaglandin-H2 d-isomerase 0.712. In addition, validation through ELISA measurements was performed. The identified proteins may serve as potential biomarkers or even targets of therapy for nAMD.

PMID: 26769219 [PubMed - as supplied by publisher]

Cell Death Differ. 2016 Jan 15. [Epub ahead of print]

Factor H uptake regulates intracellular C3 activation during apoptosis and decreases the inflammatory potential of nucleosomes.

Martin M, Leffler J, Smolağ KI, Mytych J, Björk A, Chaves LD, Alexander JJ, Quigg RJ, Blom AM.

Abstract: Factor H (FH) binds apoptotic cells to limit the inflammatory potential of complement. Here we report that FH is actively internalized by apoptotic cells to enhance cathepsin L-mediated cleavage of

endogenously expressed C3, which results in increased surface opsonization with iC3b. In addition, internalized FH forms complexes with nucleosomes, facilitates their phagocytosis by monocytes and induces an anti-inflammatory biased cytokine profile. A similar cytokine response was noted for apoptotic cells coated with FH, confirming that FH diminishes the immunogenic and inflammatory potential of autoantigens. These findings were supported by in vivo observations from CFH^{-/-} MRL-lpr mice, which exhibited higher levels of circulating nucleosomes and necrotic cells than their CFH^{+/+} littermates. This unconventional function of FH broadens the established view of apoptotic cell clearance and appears particularly important considering the strong associations with genetic FH alterations and diseases such as systemic lupus erythematosus and age-related macular degeneration.

PMID: 26768663 [PubMed - as supplied by publisher]

Int J Mol Sci. 2016 Jan 8;17(1).

NLRP3 Upregulation in Retinal Pigment Epithelium in Age-Related Macular Degeneration.

Wang Y, Hanus JW, Abu-Asab MS, Shen D, Ogilvy A, Ou J, Chu XK, Shi G, Li W, Wang S, Chan CC.

Abstract: Inflammation and oxidative stress are involved in age-related macular degeneration (AMD) and possibly associated with an activation of neuronal apoptosis inhibitor protein/class II transcription activator of the Major Histocompatibility Complex (MHC)/heterokaryon incompatibility/telomerase-associated protein 1, leucine-rich repeat or nucleotide-binding domain, leucine-rich repeat-containing family, and pyrin domain-containing 3 (NLRP3) inflammasome. In the present study, we used a translational approach to address this hypothesis. In patients with AMD, we observed increased mRNA levels of NLRP3, pro-interleukin-1 beta (IL-1 β) and pro-IL-18 in AMD lesions of the retinal pigment epithelium (RPE) and photoreceptor. In vitro, a similar increase was evoked by oxidative stress or lipopolysaccharide (LPS) stimulation in the adult retinal pigment epithelium (ARPE-19) cell line, and the increase was reduced in siRNA transfected cells to knockdown NLRP3. Ultrastructural studies of ARPE-19 cells showed a swelling of the cytoplasm, mitochondrial damage, and occurrence of autophagosome-like structures. NLRP3 positive dots were detected within autophagosome-like structures or in the extracellular space. Next, we used a mouse model of AMD, Ccl2/Cx3cr1 double knockout on rd8 background (DKO rd8) to ascertain the in vivo relevance. Ultrastructural studies of the RPE of these mice showed damaged mitochondria, autophagosome-like structures, and cytoplasmic vacuoles, which are reminiscent of the pathology seen in stressed ARPE-19 cells. The data suggest that the NLRP3 inflammasome may contribute in AMD pathogenesis.

PMID: 26760997 [PubMed - in process]

PLoS One. 2016 Jan 13;11(1):e0146808. eCollection 2016.

The COX-2-Selective Antagonist (NS-398) Inhibits Choroidal Neovascularization and Subretinal Fibrosis.

Zhang R, Liu Z, Zhang H, Zhang Y, Lin D.

Abstract: Choroidal neovascularization (CNV) is an important pathologic component of neovascular age-related macular degeneration (AMD), and CNV lesions later develop into fibrous scars, which contribute to the loss of central vision. Nowadays, the precise molecular and cellular mechanisms underlying CNV and subretinal fibrosis have yet to be fully elucidated. Cyclooxygenase-2 (COX-2) has previously been implicated in angiogenesis and fibrosis. However, the role of COX-2 in the pathogenesis of CNV and subretinal fibrosis is poorly understood. The present study reveals several important findings concerning the relationship of COX-2 signaling with CNV and subretinal fibrosis. Experimental CNV lesions were attenuated by the administration of NS-398, a COX-2-selective antagonist. NS-398-induced CNV suppression was found to be mediated by the attenuation of macrophage infiltration and down-regulation of VEGF in the retinal pigment epithelium-choroid complex. Additionally, NS-398 attenuated subretinal fibrosis, in an experimental model of subretinal scarring observed in neovascular AMD, by down-regulation

of TGF- β 2 in the retinal pigment epithelium-choroid complex. Moreover, we cultured mouse RPE cells and found that NS-398 decreased the secretion of VEGF and TGF- β 2 in mouse RPE cells. The results of the present study provide new findings regarding the molecular basis of CNV and subretinal fibrosis, and provide a proof-of-concept approach for the efficacy of COX-2 inhibition in treating subretinal fibrosis.

PMID: 26760305 [PubMed - in process]

J Exp Med. 2016 Jan 11. [Epub ahead of print]

IL-33 amplifies an innate immune response in the degenerating retina.

Xi H, Katschke K Jr, et al.

Abstract: Age-related macular degeneration (AMD), a leading cause of vision impairment in the ageing population, is characterized by irreversible loss of retinal pigment epithelial (RPE) cells and photoreceptors and can be associated with choroidal neovascularization. Mononuclear phagocytes are often present in AMD lesions, but the processes that direct myeloid cell recruitment remain unclear. Here, we identify IL-33 as a key regulator of inflammation and photoreceptor degeneration after retina stress or injury. IL-33+ Müller cells were more abundant and IL-33 cytokine was elevated in advanced AMD cases compared with age-matched controls with no AMD. In rodents, retina stress resulted in release of bioactive IL-33 that in turn increased inflammatory chemokine and cytokine expression in activated Müller cells. Deletion of ST2, the IL-33 receptor α chain, or treatment with a soluble IL-33 decoy receptor significantly reduced release of inflammatory mediators from Müller cells, inhibited accumulation of mononuclear phagocytes in the outer retina, and protected photoreceptor rods and cones after a retina insult. This study demonstrates a central role for IL-33 in regulating mononuclear phagocyte recruitment to the photoreceptor layer and positions IL-33 signaling as a potential therapeutic target in macular degenerative diseases.

PMID: 26755704 [PubMed - as supplied by publisher]

Genetics

JAMA Ophthalmol. 2016 Jan 14:1-8. [Epub ahead of print]

Rare Genetic Variants Associated With Development of Age-Related Macular Degeneration.

Saksens NT, Geerlings MJ, Bakker B, Schick T, Daha MR, Fauser S, Boon CJ, de Jong EK, Hoyng CB, den Hollander AI.

IMPORTANCE: Rare variants in the complement genes CFH, CFI, C9, and C3 have been found to be highly associated with age-related macular degeneration (AMD); however, the effect on clinical characteristics and familial segregation by these variants is lacking.

OBJECTIVES: To determine the contribution of rare CFH Arg1210Cys, CFI Gly119Arg, C9 Pro167Ser, and C3 Lys155Gln variants in the development of AMD in 22 multiplex families and to describe clinical differences in carriers vs noncarriers in these families and a large case-control cohort.

DESIGN, SETTING, AND PARTICIPANTS: This retrospective case-control study included 114 affected and 60 unaffected members of 22 multiplex families with AMD as well as 1589 unrelated patients with AMD and 1386 unrelated control individuals enrolled in the European Genetic Database (EUGENDA). Patients were recruited from March 29, 2006, to April 26, 2013, and data were collected from April 20, 2012, to May 7, 2014. All participants underwent an extensive ophthalmic examination and completed a questionnaire. Venous blood samples were obtained from all participants for genetic analysis, including whole-exome sequencing and measurements of complement activation. Data were analyzed from September 23, 2014, to November 4, 2015.

MAIN OUTCOMES AND MEASURES: Differences between carriers and noncarriers of rare variants in age

at onset of symptoms, the family history of AMD, complement activation levels (C3d:C3 ratio), the presence of reticular pseudodrusen, and AMD phenotype.

RESULTS: Among the 114 affected and 60 unaffected members of 22 multiplex families with AMD and the 1598 unrelated patients with AMD and 1386 controls in the EUGENDA cohort who underwent analysis, the presence of the CFI Gly119Arg, C9 Pro167Ser, or C3 Lys155Gln variant was confirmed in 18 individuals in 5 families but did not completely segregate with the disease. In the case-control cohort, the 91 affected carriers of these variants were younger at symptom onset (mean [SD] age, 67.4 [8.5] vs 71.3 [8.9] years; $P = .01$) and more often reported a positive family history (35 of 79 [44.3%] vs 367 of 1201 [30.6%]; $P = .008$) compared with the 1498 noncarriers. Patients with advanced atrophic AMD carried these rare variants more frequently than patients with neovascular AMD (11 of 93 [11.8%] vs 40 of 835 [4.8%]; $P = .04$).

CONCLUSIONS AND RELEVANCE: Previously reported rare variants do not completely segregate within families with AMD. However, patients carrying these rare variants differ clinically from noncarriers by an earlier age at symptom onset, higher prevalence of a positive family history, and AMD phenotype. These results suggest that genetic tests for AMD might be designed to detect common and rare genetic variants, especially in families, because rare variants contribute to the age at onset and progression of the disease.

PMID: 26767664 [PubMed - as supplied by publisher]

Environ Mol Mutagen. 2016 Jan;57(1):58-64. Epub 2015 Sep 10.

Functional single nucleotide polymorphism in IL-17A 3' untranslated region is targeted by miR-4480 in vitro and may be associated with age-related macular degeneration.

Popp NA, Yu D, Green B, Chew EY, Ning B, Chan CC, Tuo J.

Abstract: Age-related macular degeneration (AMD) is a leading cause of irreversible central vision loss in the elderly. Genetic factors contributing to AMD include single nucleotide polymorphisms (SNPs) in immune-related genes including CFH, C2, CFI, C9, and C3, thus implicating these pathways in AMD pathogenesis. MicroRNAs (miRNAs) are powerful regulators of gene expression and execute this function by binding to the 3' untranslated region (3'UTR) of target mRNAs, leading to mRNA degradation. In this study, we searched for the possible association of SNPs in the 3'UTR region of IL-17A, a gene implicated in AMD pathogenesis without any previous SNP association with AMD. Using two independent sample cohorts of Caucasian subjects, six SNPs in the IL-17A 3'-UTR were selected for genotyping based on bioinformatic predictions of the SNP effect on microRNA binding. The SNP rs7747909 was found to be associated with AMD ($P < 0.05$) in the NEI cohort, using a dominant model logistic regression. Luciferase reporter gene assays and RNA electrophoretic mobility shift assays were performed using ARPE-19 cells to confirm the preferential binding of microRNAs to the major allele of the SNP. Our findings support the hypothesis that microRNA-mediated gene dysregulation may play a role in the pathogenesis of AMD. *Environ. Mol. Mutagen.* 57:58-64, 2016. © 2015 Wiley Periodicals, Inc.

PMID: 26765636 [PubMed - in process]

Hum Gene Ther. 2016 Jan 11. [Epub ahead of print]

Let there be light: gene and cell therapy for blindness.

Dalkara D, Goureau O, Marazova K, Sahel JA.

Abstract: Retinal degenerative diseases are a leading cause of irreversible blindness. Retinal cell death is the main cause of vision loss in genetic disorders such as retinitis pigmentosa, Stargardt disease and Leber congenital amaurosis, as well as in complex age-related diseases such as age-related macular degeneration (AMD). For these blinding conditions, gene and cell therapy approaches offer therapeutic intervention at various disease stages. The present review outlines recent advances in therapies for retinal degenerative disease, focusing on the progress and challenges in the development and clinical translation

of gene and cell therapies. A significant body of preclinical evidence and initial clinical results pave the way for further development of these cutting edge treatments for patients with retinal degenerative disorders.

PMID: 26751519 [PubMed - as supplied by publisher]

Diet, lifestyle & low vision

Clin Ophthalmol. 2015 Dec 30;10:55-63. eCollection 2016.

Anxiety and depression in patients with advanced macular degeneration: current perspectives.

Cimarolli VR, Casten RJ, Rovner BW, Heyl V, Sørensen S, Horowitz A.

Abstract: Age-related macular degeneration (AMD) - despite advances in prevention and medical treatment options - remains prevalent among older adults, often resulting in functional losses that negatively affect the mental health of older adults. In particular, the prevalence of both anxiety and depression in patients with AMD is high. Along with medical treatment options, low vision rehabilitation and AMD-specific behavioral and self-management programs have been developed and have demonstrated effectiveness in improving the mental health of AMD patients. This article reviews the prevalence of anxiety and depression in patients with advanced AMD, discusses potential mechanisms accounting for the development of depression and anxiety in AMD patients, presents the state-of-the-art of available interventions for addressing anxiety and depression in AMD patients, and delineates recommendations for eye care professionals regarding how to screen for these two prevalent mental health problems and how to facilitate appropriate treatment for patients with AMD.

PMID: 26766899 [PubMed]

J Lipid Res. 2016 Jan 13. [Epub ahead of print]

Associations of Human Retinal Very Long-chain Polyunsaturated Fatty Acids with Dietary Lipid Biomarkers.

Gorusupudi A, Liu A, Hageman GS, Bernstein PS.

Abstract: The human retina is well-known to have unique lipid profiles enriched in long-chain polyunsaturated fatty acids (LC-PUFAs) and very long-chain polyunsaturated fatty acids (VLC-PUFAs) that appear to promote normal retinal structure and function, but the influence of diet on retinal lipid profiles in health and disease remains controversial. In this study, we examined two independent cohorts of donor eyes and related their retinal lipid profiles with systemic biomarkers of lipid intake. We found that serum and red blood cell lipids, and to a lesser extent orbital fat, are indeed excellent biomarkers of retinal lipid content and n-3/n-6 ratios in both the LC-PUFA and VLC-PUFA series. Eyes from age-related macular degeneration (AMD) donors have significantly decreased levels of VLC-PUFAs and low n-3/n-6 ratios. These results are consistent with the protective role of dietary n-3 LC-PUFAs against AMD and emphasize the importance of monitoring systemic biomarkers of lipid intake when undertaking clinical trials of lipid supplements for prevention and treatment of retinal disease.

PMID: 26764040 [PubMed - as supplied by publisher]

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