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MD Research News

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Drug treatment

Graefes Arch Clin Exp Ophthalmol. 2015 Mar 7. [Epub ahead of print]

Pigment epithelial tears after ranibizumab injection in polypoidal choroidal vasculopathy and typical age-related macular degeneration.

Shin JY, Choi M, Chung B, Byeon SH.

PURPOSE: The purpose of the study was to compare the rates and characteristics of retinal pigment epithelial (RPE) tears between typical exudative age-related macular degeneration (tAMD) and polypoidal choroidal vasculopathy (PCV) after injection of intravitreal ranibizumab (IVR).

METHODS: In total, 836 eyes from 784 patients with exudative AMD treated with IVR were analyzed. The presence, type, size, and height of pigment epithelial detachment (PED) in OCT before injection were evaluated, and the occurrence rate of RPE tears within three months of injection between tAMD and PCV was compared.

RESULTS: In total, 515 eyes (61.6 %) had tAMD and 321 eyes (38.4 %) were diagnosed as PCV. RPE tears developed in 18 eyes (3.5 %) in the tAMD group, while only two eyes (0.62 %) were associated with PCV ($p = 0.009$, Chi-square test). Eleven of the eighteen eyes with RPE tears in tAMD had fibrovascular PED with contractile neovascular tissue under the surface of the RPE and a cleft at baseline. Two eyes with RPE tears in PCV showed large hemorrhagic PED before presenting with an RPE tear.

CONCLUSIONS: RPE tears after IVR were significantly less common in PCV than in tAMD. The different characteristics of RPE tears between the two disease entities suggest differences in the pathogenesis underlying the event.

PMID: 25744335 [PubMed - as supplied by publisher]

Rev Col Bras Cir. 2014 Nov-Dec;41(6):386-92.

CFH Y402H polymorphism and response to intravitreal Ranibizumab in Brazilian patients with neovascular age-related macular degeneration.[Article in English, Portuguese]

Veloso CE, Almeida LN, Nehemy MB.

OBJECTIVE: To investigate the association between CFH gene polymorphism and response to ranibizumab in Brazilian patients with neovascular age-related macular degeneration (AMD).

METHODS: 95 patients were genotyped for the CFH rs1061170 (Y402H) single nucleotide polymorphism. Patients with neovascular AMD initially received intravitreal ranibizumab injections for three months and were retreated as needed. Visual acuity (VA) and central retinal thickness (CRT) were measured before treatment and at 1, 3, 6, and 12 months post-treatment.

RESULTS: For patients with the TT and TC genotypes, paired comparisons of VA showed a statistically significant improvement when the data obtained at all visits were compared with baseline. Patients homozygous for the risk genotype (CC) did not show a statistically significant improvement when VA obtained at visits 1, 3, 6 and 12 were compared with baseline. For all genotypes, paired comparisons of CRT showed a statistically significant improvement when the data obtained at visits 1, 3, 6 and 12 were compared with baseline.

CONCLUSION: Patients with the CC genotype showed poorer long-term functional response to intravitreal ranibizumab.

PMID: 25742403 [PubMed - in process]

Br J Ophthalmol. 2015 Mar 4. [Epub ahead of print]

Compatibility of recombinant tissue plasminogen activator (rtPA) and aflibercept or ranibizumab coapplied for neovascular age-related macular degeneration with submacular haemorrhage.

Klettner A, Grotelüschen S, Treumer F, Roider J, Hillenkamp J.

BACKGROUND/AIMS: Subretinal coapplication of recombinant tissue plasminogen activator (rtPA) and vascular endothelial growth factor (VEGF)-antagonists is a new treatment option for age-related macular degeneration complicated by submacular haemorrhage. Here, we investigate the compatibility of rtPA and aflibercept or ranibizumab in vitro because intraoperatively, rtPA or rtPA-induced plasmin may cleave aflibercept or ranibizumab.

METHODS: Aflibercept and ranibizumab, respectively, were incubated with rtPA or plasmin, separated in gel electrophoresis and stained with Coomassie or silver. The antiangiogenic activity of the VEGF-antagonists was quantified by VEGF-ELISA after incubation with the supernatant of primary porcine retinal pigment epithelium cell cultures.

RESULTS: In electrophoresis, ranibizumab displayed no additional fragments when it was coapplied with rtPA or plasmin. Its VEGF-inhibiting efficacy remained unchanged in coapplication with rtPA with or without blood, or plasmin. rtPA did not cleave or functionally compromise aflibercept. When aflibercept was coapplied with plasmin, electrophoresis displayed additional bands in Coomassie (30 kDa, 27 kDa, 19 kDa, 15 kDa) and silver staining (31 kDa, 26 kDa, 21 kDa, 19 kDa, 15 kDa). While at a clinical dosage (800 µg/mL) VEGF was inhibited by aflibercept when coapplied with plasmin, at borderline concentrations (400 ng/mL) VEGF-binding ability of aflibercept was abolished.

CONCLUSIONS: Ranibizumab is not cleaved or functionally compromised by rtPA or plasmin. Aflibercept is cleaved and its VEGF-binding ability is reduced when coapplied with plasmin. In clinical practice, rtPA and ranibizumab can be coapplied as a treatment for neovascular age-related macular degeneration with submacular haemorrhage while the antiangiogenic activity of aflibercept may be compromised when coapplied with rtPA in the presence of plasmin.

PMID: 25740806 [PubMed - as supplied by publisher]

Diabetes Metab J. 2015 Feb;39(1):46-50. doi: 10.4093/dmj.2015.39.1.46. Epub 2015 Feb 16.

Intravitreal ranibizumab for subfoveal choroidal neovascularization from age-related macular degeneration with combined severe diabetic retinopathy.

Han SY, Bae JH, Oh J, Yu HG, Song SJ

BACKGROUND: To evaluate the efficacy of intravitreal ranibizumab for subfoveal choroidal neovascularization (CNV) from age-related macular degeneration (AMD) with combined severe diabetic retinopathy (DR).

METHODS: This retrospective, interventional case series included eleven patients (mean age, 70.09 years; range, 54 to 83 years) with at least severe non-proliferative DR and subfoveal CNV secondary to AMD. Each subject was treated with intravitreal injections of 0.5 mg ranibizumab. The primary outcomes included change in best-corrected visual acuity and central subfield thickness (CST) on optical coherence tomography (OCT).

RESULTS: The mean follow-up time was 16.7±14 months (range, 6 to 31 months). Mean visual acuity improved from 1.21±0.80 logarithm of the minimum angle of resolution (logMAR) to 1.0±0.6 logMAR (P=0.107), 0.95±0.62 logMAR (P=0.044), 1.10±0.68 logMAR (P=0.296), and 1.13±0.66 logMAR (P=0.838) at 1, 3, 6, and 12 months after injection, respectively. Eight patients (72.7%) gained or maintained vision (mean 0.32 logMAR), whereas three patients (27.3%) lost more than one line of vision (mean 0.51 logMAR). The mean OCT CST was 343.9±134.6 μm at baseline, and the mean CST at 1, 3, 6, 12 months after the injection was 367.8±172.1 (P=0.864), 346.2±246.2 (P=0.857), 342±194.1 (P=0.551), and 294.2±108.3 μm (P=0.621), respectively.

CONCLUSION: Intravitreal ranibizumab injection can be considered to be a therapy for the stabilization of subfoveal CNV secondary to AMD with combined severe DR. However, these patients might exhibit limited visual improvement after treatment.

PMID: 25729712 [PubMed] PMCID: PMC4342536

Br J Ophthalmol. 2015 Mar 4. [Epub ahead of print]

Ranibizumab for subfoveal choroidal neovascularisation associated with Stargardt disease.

Battaglia Parodi M, Munk MR, Iacono P, Bandello F.

INTRODUCTION: To describe the clinical outcomes of intravitreal ranibizumab treatment for subfoveal choroidal neovascularisation (CNV) associated with Stargardt disease.

METHODS: Prospective, interventional, case series. All patients underwent intravitreal ranibizumab injections following a pro re nata regimen with monthly examination, over a 24-month follow-up.

RESULTS: Three eyes were included in the study. Best corrected visual acuity changed from 0.47±0.06 (mean±SD) at baseline to 0.90±0.17 LogMAR at the end of the 24-month follow-up. Overall, a mean number of 11 ranibizumab injections were administered in 24 months. Significant atrophic growth was detected in all cases, with the mean atrophy area increasing from 2.34±2.60 mm2 (mean±SD) at baseline to 4.23±3.31 mm2 at the end of the follow-up.

CONCLUSIONS: Ranibizumab treatment can stop the CNV progression, but cannot ensure a significant visual improvement. Macular atrophy tends to significantly enlarge under ranibizumab treatment over the follow-up.

PMID: 25740804 [PubMed - as supplied by publisher]

Jpn J Ophthalmol. 2015 Mar 4. [Epub ahead of print]

Long-term outcome of intravitreal pegaptanib sodium as maintenance therapy in Japanese patients with neovascular age-related macular degeneration.

Inoue M, Kadonosono K, Arakawa A, Yamane S, Ishibashi T

PURPOSE: To evaluate the results of a 3-year follow-up of intravitreal pegaptanib sodium injection as maintenance therapy for the treatment of neovascular age-related macular degeneration (AMD) in Japanese patients.

METHODS: In this prospective, uncontrolled interventional study, 20 eyes of 19 patients with treatment-naïve AMD who had received 3 consecutive monthly injections of 0.5 mg/0.05 mL ranibizumab as the induction treatment and had shown clinical/anatomical improvement were enrolled. An intravitreal injection of 0.3 mg/0.09 mL pegaptanib sodium was administered as the maintenance therapy every 6 weeks. Booster treatments using ranibizumab were allowed if clinical deterioration was judged to be present. The primary outcome measures were the best-corrected visual acuity (BCVA) and the central foveal thickness (CFT) as evaluated using spectral-domain optical coherence tomography.

RESULTS: Sixteen of the 20 eyes (80 %) were assessed at the 3-year follow-up. The mean logMAR BCVA improved significantly from 0.56 ± 0.31 before the induction treatment to 0.24 ± 0.25 at baseline ($P < 0.001$) and was well maintained at 156 weeks (0.25 ± 0.28, $P = 0.938$). Moreover, the mean CFT also decreased significantly from 346 ± 111 μm before the induction treatment to 232 ± 54 μm at baseline ($P < 0.001$) and was well preserved at 156 weeks (210 ± 59 μm, $P = 0.278$). Thirteen eyes (81.3 %) received an unscheduled booster treatment, and no severe systemic or ocular side effects occurred during follow-up.

CONCLUSION: Intravitreal pegaptanib sodium injection as the maintenance therapy was effective in stabilizing the vision of patients with AMD in whom induction treatment led to improved BCVA, as evaluated at the 3-year follow-up.

PMID: 25733493 [PubMed - as supplied by publisher]

Ophthalmologe. 2015 Mar 6. [Epub ahead of print]

[Anti-VEGF therapy for neovascular age-related macular degeneration -therapeutic strategies : Statement of the German Ophthalmological Society, the German Retina Society and the Professional Association of Ophthalmologists in Germany - November 2014.][Article in German]

Deutsche Ophthalmologische Gesellschaft.

PMID: 25739373 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Invest Ophthalmol Vis Sci. 2015 Mar 3. [Epub ahead of print]

Impact of Reticular Pseudodrusen on Microperimetry and Multifocal Electroretinography in Intermediate Age-Related Macular Degeneration.

Wu Z, Ayton LN, Makeyeva G, Guymer RH, Luu CD.

Purpose: To examine the influence of reticular pseudodrusen (RPD) on retinal and visual function in intermediate age-related macular degeneration (AMD) using multifocal electroretinography (mfERG) and microperimetry.

Methods: In a prospective cross-sectional study, microperimetry and mfERG testing, followed by colour fundus photography, near-infrared reflectance imaging and spectral-domain optical coherence tomography (SD-OCT) scans were performed in 120 eyes from 60 participants with bilateral intermediate AMD. The number of subfields with pigmentary changes and RPD within the central 3 mm diameter of the Early Treatment of Diabetic Retinopathy Study (ETDRS) grid and drusen cube root volume within the central 3 mm diameter was determined. The influence of these pathological features on microperimetry and mfERG

in this region were examined.

Results: Microperimetric sensitivity was not significantly associated with the presence and extent of RPD (P = 0.068), but with drusen volume and extent of pigmentary changes (P < 0.001 for both). However, the presence and extent of RPD was independently and significantly associated with mfERG implicit time, along with drusen volume and the extent of pigmentary changes (P ≤ 0.023). The mfERG response amplitude was not significantly associated with the presence and extent of RPD (P = 0.130).

Conclusions: The presence and extent of RPD was associated with functional changes on mfERG implicit time, but not mfERG response amplitude or microperimetry. These findings suggest that the presence of RPD in eyes with intermediate AMD has a significant influence on cone-mediated neuroretinal function, without a significant influence on mesopic visual function as determined on microperimetry.

PMID: 25736790 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2015 Mar 3. pii: IOVS-14-16069. doi: 10.1167/iovs.14-16069. [Epub ahead of print]

Functional visual improvement after cataract surgery in eyes with age-related macular degeneration; Results of the Ophthalmic Surgical Outcomes Data (OSOD) Project.

Stock MV, Vollman DE, Baze EF, Chomsky AS, Daly MK, Lawrence M

Purpose: To determine if cataract surgery on eyes with age-related macular degeneration (AMD) confers as much functional visual improvement as on eyes without retinal pathology.

Methods: This is a retrospective analysis of 4,924 cataract surgeries from the VA Ophthalmic Surgical Outcomes Data Project. We included cases of eyes with AMD which had both preoperative and postoperative NEI-VFQ-25 questionnaires submitted and compared their outcomes to controls without retinal pathology. We excluded patients with other retinal pathologies. The analyses compared changes in visual acuity and overall functional visual improvement and its subscales.

Results: Preoperative and postoperative questionnaires were submitted by 58.3% of AMD and 63.8% of controls. Analysis of overall score showed that cataract surgery on eyes with AMD led to increased visual function (13.8± 2.4 NEI-VFQ units, P<0.0001); however, increases were significantly less when compared to controls (-6.4± 2.9 NEI-VFQ units, P<0.0001). Preoperative best corrected visual acuity (preBCVA) in AMD was predictive of postoperative visual function (r=-0.38, P<0.0001). In controls, postoperative visual function was only weakly associated with preBCVA (r=-0.075, P=0.0002). AMD patients with vision of 20/40 or better had overall outcomes similar to controls (-2.2± 4.7 NEI-VFQ units, P=0.37).

Conclusions: Cataract surgery on eyes with AMD offers an increase in functional visual improvement; however, the amount of benefit is associated with the eye's preBCVA. For eyes with preBCVA ≥20/40, the improvement is similar to that of patients without retinal pathology. However, if preBCVA is <20/40, the amount of improvement was shown to be significantly less and decreased with decreasing preBCVA.

PMID: 25736786 [PubMed - as supplied by publisher]

Eur J Pharm Biopharm. 2015 Feb 25. [Epub ahead of print]

Antibody therapies and their challenges in the treatment of age-related macular degeneration.

Volz C, Pauly D.

Abstract: Age-related macular degeneration (AMD) is the leading cause of vision loss in the western world. This multifactorial disease results from the combined contributions of age, environment and genetic predisposition. Antibody-based treatment of late-stage neovascular AMD with inhibitors of vascular

endothelial growth factor has had great success, which is now the goal for currently untreatable AMD manifestations. The existence of an immune-privileged environment in the eye supports the feasibility of localized antibody therapy. Many different antibodies against various targets are being developed for the treatment of AMD, which reflects the etiological complexity of the disease. This review provides an overview of 19 potential therapeutic antibodies targeting angiogenesis, the complement system, inflammation or amyloid beta deposition in the eye. It summarizes the immunoglobulin structure, the specific target and study outcomes for each approach. The latter include beneficial results or adverse effects in AMD models and patients. Finally, this article discusses the challenges in the development of antibody-based drugs to treat degenerative processes in the posterior eye. In spite of these difficulties, to date, the following four antibodies have overcome the technical and preclinical hurdles and are being tested in active clinical studies: Lampalizumab, Sonepcizumab, GSK933776 and LFG316. We conclude that, while there are some antibody-based drugs that have made it into clinical practice, a successful transfer from bench to beside is still pending for many promising approaches.

PMID: 25725263 [PubMed - as supplied by publisher]

Eur J Hum Genet. 2015 Mar 4. doi: 10.1038/ejhg.2015.25. [Epub ahead of print]

Kullback-Leibler divergence for detection of rare haplotype common disease association.

Lin S.

Abstract: Rare haplotypes may tag rare causal variants of common diseases; hence, detection of such rare haplotypes may also contribute to our understanding of complex disease etiology. Because rare haplotypes frequently result from common single-nucleotide polymorphisms (SNPs), focusing on rare haplotypes is much more economical compared with using rare single-nucleotide variants (SNVs) from sequencing, as SNPs are available and 'free' from already amassed genome-wide studies. Further, associated haplotypes may shed light on the underlying disease causal mechanism, a feat unmatched by SNV-based collapsing methods. In recent years, data mining approaches have been adapted to detect rare haplotype association. However, as they rely on an assumed underlying disease model and require the specification of a null haplotype, results can be erroneous if such assumptions are violated. In this paper, we present a haplotype association method based on Kullback-Leibler divergence (hapKL) for case-control samples. The idea is to compare haplotype frequencies for the cases versus the controls by computing symmetrical divergence measures. An important property of such measures is that both the frequencies and logarithms of the frequencies contribute in parallel, thus balancing the contributions from rare and common, and accommodating both deleterious and protective, haplotypes. A simulation study under various scenarios shows that hapKL has well-controlled type I error rates and good power compared with existing data mining methods. Application of hapKL to age-related macular degeneration (AMD) shows a strong association of the complement factor H (CFH) gene with AMD, identifying several individual rare haplotypes with strong signals.

PMID: 25735482 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2015 Feb 17;9:353-66.

Strategies for improving early detection and diagnosis of neovascular age-related macular degeneration.

Keane PA, de Salvo G, Sim DA, Goverdhan S, Agrawal R, Tufail A

Abstract: Treatment of the neovascular form of age-related macular degeneration (AMD) has been revolutionized by the introduction of such agents as ranibizumab, bevacizumab, and aflibercept. As a result, the incidence of legal blindness occurring secondary to AMD has fallen dramatically in recent years in many countries. While these agents have undoubtedly been successful in reducing visual impairment and blindness, patients with neovascular AMD typically lose some vision over time, and often lose the ability to

read, drive, or perform other important activities of daily living. Efforts are therefore under way to develop strategies that allow for earlier detection and treatment of this disease. In this review, we begin by providing an overview of the rationale for, and the benefits of, early detection and treatment of neovascular AMD. To achieve this, we begin by providing an overview of the pathophysiology and natural history of choroidal neovascularization, before reviewing the evidence from both clinical trials and "real-world" outcome studies. We continue by highlighting an area that is often overlooked: the importance of patient education and awareness for early AMD detection. We conclude the review by reviewing an array of both established and emerging technologies for early detection of choroidal neovascularization, ranging from Amsler chart testing, to hyperacuity testing, to advanced imaging techniques, such as optical coherence tomography.

PMID: 25733802 [PubMed] PMCID: PMC4337735

Pathogenesis

Graefes Arch Clin Exp Ophthalmol. 2015 Mar 7. [Epub ahead of print]

Plasma levels of amyloid beta and other proinflammatory mediators in patients with age-related macular degeneration.

Guymer R, Cipriani T, Rittenhouse KD, Lim L, Robman LD, Li W, Wang W, Deng S, Banerjee P.

PURPOSE: To investigate the plasma levels of amyloid beta (Aβ) and select inflammatory mediators in patients with various stages of AMD compared to that of age-matched controls, and discern a relationship to disease severity.

METHODS: Plasma samples were obtained from AMD subjects at various stages of disease-early (drusen only), geographic atrophy (GA), neovascular AMD (CNV)-and from controls of similar age without AMD. Samples were analyzed using a commercially available ELISA kit (sixteen cytokines) or LC/MS/MS (Aβ isotypes). Descriptive statistics were compiled on all analytes. Analysis of covariance (ANCOVA) was conducted to compare each analyte across AMD groups while adjusting for sex and age of the patients, and in comparison to the control group. Receiver operating characteristics plots were generated for the strongest predictor variables.

RESULTS: Levels of alternative spliced CC3 proteins were significantly different between controls and CNV groups ($p < 0.05$), with median levels almost twice higher in CNV than in controls. There was an increasing trend for plasma levels of Aβ isotypes across AMD progressive stages (p values ranged from 0.052 to 0.0012) (ANCOVA). When adjusted for multiple comparisons analysis, plasma Aβ 1-42 levels, and its ratio with Aβ 1-40 were the most significantly associated with late AMD stages. Consistently with the ANCOVA results for Aβ isotypes, the ROC curve showed a moderate prediction (AUC = - ~ 0.78) of AMD vs control using the Aβ 1-42 isotype.

CONCLUSION: Plasma Aβ 1-42 may have utility as a systemic biomarker for AMD.

PMID: 25744331 [PubMed - as supplied by publisher]

Korean J Physiol Pharmacol. 2015 Mar;19(2):167-75.

Effect of Stimulus Waveform of Biphasic Current Pulse on Retinal Ganglion Cell Responses in Retinal Degeneration (rd1) mice.

Ahn KN, Ahn JY, Kim JH, Cho K, Koo KI, Senok SS, Goo YS.

Abstract: A retinal prosthesis is being developed for the restoration of vision in patients with retinitis pigmentosa (RP) and age-related macular degeneration (AMD). Determining optimal electrical stimulation parameters for the prosthesis is one of the most important elements for the development of a viable retinal

prosthesis. Here, we investigated the effects of different charge-balanced biphasic pulses with regard to their effectiveness in evoking retinal ganglion cell (RGC) responses. Retinal degeneration (rd1) mice were used (n=17). From the ex-vivo retinal preparation, retinal patches were placed ganglion cell layer down onto an 8×8 multielectrode array (MEA) and RGC responses were recorded while applying electrical stimuli. For asymmetric pulses, 1st phase of the pulse is the same with symmetric pulse but the amplitude of 2nd phase of the pulse is less than 10 μA and charge balanced condition is satisfied by lengthening the duration of the pulse. For intensities (or duration) modulation, duration (or amplitude) of the pulse was fixed to 500 μs (30 μA), changing the intensities (or duration) from 2 to 60 μA (60 to 1000 μs). RGCs were classified as response-positive when PSTH showed multiple (3~4) peaks within 400 ms post stimulus and the number of spikes was at least 30% more than that for the immediate pre-stimulus 400 ms period. RGC responses were well modulated both with anodic and cathodic phase-1st biphasic pulses. Cathodic phase-1st pulses produced significantly better modulation of RGC activity than anodic phase-1st pulses regardless of symmetry of the pulse.

PMID: 25729279 [PubMed] PMCID: PMC4342737

Stem Cells. 2015 Feb 28. [Epub ahead of print]

Protective effects of human iPS-derived retinal pigmented epithelial cells in comparison with human mesenchymal stromal cells and human neural stem cells on the degenerating retina in rd1 mice.

Sun J, Mandai M, Kamao H, Hashiguchi T, Shikamura M, Kawamata S, Sugita S, Takahashi M

Abstract: Retinitis pigmentosa (RP) is a group of visual impairments characterized by progressive rod photoreceptor cell loss due to a genetic background. Pigment epithelium-derived factor (PEDF) predominantly secreted by the retinal pigmented epithelium (RPE) has been reported to protect photoreceptors in retinal degeneration models, including rd1. In addition, clinical trials are currently underway outside Japan using human mesenchymal stromal cells (MSCs) and human neural stem cells (NSCs) to treat RP and dry age-related macular degeneration (AMD), respectively. Thus, the present study aimed to investigate the rescue effects of induced pluripotent stem (iPS)-RPE cells in comparison with those cells in a clinical trial on photoreceptor degeneration in rd1 mice. Cells were injected into the subretinal space of immune-suppressed 2-week-old rd1 mice. The results demonstrated that human iPS-RPE cells significantly attenuated photoreceptor degeneration on postoperative days (PODs) 14 and 21 and survived longer up to at least 12 weeks after operation than the other two types of graft cells with less immune responses and apoptosis. The mean PEDF concentration in the intraocular fluid (IF) in RPE-transplanted eyes was over 1 μg/ml at PODs 14 and 21, and this may have contributed to the protective effect of RPE transplantation. Our findings suggest that iPS-RPE cells serve as a competent source to delay photoreceptor degeneration through stable survival in degenerating ocular environment and by releasing neuroprotective factors such as PEDF.

PMID: 25728228 [PubMed - as supplied by publisher]

JAMA Ophthalmol. 2015 Mar 5. [Epub ahead of print]

Clinicopathological Correlation of Outer Retinal Tubulation in Age-Related Macular Degeneration.

Litts KM, Messinger JD, Dellatorre K, Yannuzzi LA, Freund KB, Curcio CA.

PMID: 25742505 [PubMed - as supplied by publisher]

Genetics

J Clin Med. 2015 Jan 1;4(1):18-31.

Role of Factor H and Related Proteins in Regulating Complement Activation in the Macula, and Relevance to Age-Related Macular Degeneration.

Clark SJ, Bishop PN.

Abstract: The recent revolution in age-related macular degeneration (AMD) genetics has demonstrated that genetic alterations affecting the alternative pathway of the complement cascade have a major influence on AMD risk. One of the two most important genetic loci is on chromosome 1 and contains genes encoding complement factor H (FH) and the factor H related proteins (FHR proteins). In macular tissue, especially Bruch's membrane, relatively high levels of a truncated splice variant of FH called factor H-like protein 1 (FHL-1) are present. Here we discuss how genetic variations may alter the amounts, or by altering their protein sequences, the functions of these proteins. In particular, the common Y402H polymorphism affects the ability of FHL-1 and FH to localize to Bruch's membrane and the inner choroid because it alters the ability of these complement regulators to bind heparan sulphate (HS) in these structures. In addition, there is an age-related loss of HS from Bruch's membrane. We hypothesize that a combination of poor binding of the 402H variants of FHL-1 and FH to Bruch's membrane, combined with a decrease in binding due to age-related HS loss, eventually results in insufficient FHL-1 and FH binding to Bruch's membrane. This could result in complement activation, inflammation and thereby predispose to AMD.

PMID: 25729613 [PubMed] PMCID: PMC4340553

Sci Rep. 2015 Mar 3;5:8709.

C2 rs547154 polymorphism and polypoidal choroidal vasculopathy susceptibility: a meta-analysis.

Chen X, Kang X, Zhao K, Zhao C.

Abstract: Previous studies have indicated the association between C2 rs547154 polymorphism and polypoidal choroidal vasculopathy (PCV) risk, while the results are controversial and inconsistent. Herein, we perform a meta-analysis to gain a precise estimation of the association using 5 eligible studies involving 4076 subjects, of which 1220 were PCV cases, 1073 were age-related macular degeneration (AMD) cases and 1783 were controls. Allelic frequencies of C2 rs547154 polymorphism between PCV and AMD were also compared. Both crude and adjusted odds ratios (OR) with their 95% confidence interval (CI) were included to assess the strength of the association. The pooled OR in random-effect model for allele T versus G was 0.64 (95% CI, 0.52-0.80; p < 0.0001), for genotype TG versus GG was 0.65 (95% CI, 0.52-0.83; p, 0.0004), and for genotype TT + TG versus GG was 0.64 (95% CI, 0.51-0.80; p, 0.0002). No difference in allelic frequency was observed between PCV and AMD (OR, 0.86; 95% CI, 0.64-1.16; p, 0.32). Sensitivity analysis proved the robustness of our data. No significant ethnic divergence was suggested by subgroup analysis, and no publication bias was detected via Egger's test. In conclusion, our data indicate that C2 rs547154 polymorphism plays a protective role in the development of PCV.

PMID: 25732348 [PubMed - in process]

Diet, lifestyle & low vision

Med Hypothesis Discov Innov Ophthalmol. 2014 Fall;3(3):83-90.

Physiology and psychology of vision and its disorders: a review.

Moschos MM.

Abstract: The purpose of this review is to bring together to the physiology and psychology of vision and to analyze, based on our own data and on the available literature, the relationship between sight loss and individual reactions. As recent treatments for depression are often effective and have few side-effects, ophthalmologists should consider referral for treatment of depression in patients suffering from vision impairment. For this reason, vision rehabilitation should be more readily available and recommended.

PMID: 25741524 [PubMed]

Patient. 2015 Mar 1. [Epub ahead of print]

Focus Groups in Elderly Ophthalmologic Patients: Setting the Stage for Quantitative Preference Elicitation.

Danner M, Vennedey V, Hiligsmann M, Fauser S, Stock S

OBJECTIVES: Patients suffering from age-related macular degeneration (AMD) are rarely actively involved in decision-making, despite facing preference-sensitive treatment decisions. This paper presents a qualitative study to prepare quantitative preference elicitation in AMD patients. The aims of this study were (1) to gain familiarity with and learn about the special requirements of the AMD patient population for quantitative data collection; and (2) to select/refine patient-relevant treatment attributes and levels, and gain insights into preference structures.

METHODS: Semi-structured focus group interviews were performed. An interview guide including preselected categories in the form of seven potentially patient-relevant treatment attributes was followed. To identify the most patient-relevant treatment attributes, a ranking exercise was performed. Deductive content analyses were done by two independent reviewers for each attribute to derive subcategories (potential levels of attributes) and depict preference trends.

RESULTS: The focus group interviews included 21 patients. The interviews revealed that quantitative preference surveys in this population will have to be interviewer assisted to make the survey feasible for patients. The five most patient-relevant attributes were the effect on visual function [ranking score (RS): 139], injection frequency (RS: 101), approval status (RS: 83), side effects (RS: 79), and monitoring frequency (RS: 76). Attribute and level refinement was based on patients' statements. Preference trends and dependencies between attributes informed the quantitative instrument design.

CONCLUSION: This study suggests that qualitative research is a very helpful step to prepare the design and administration of quantitative preference elicitation instruments. It especially facilitated familiarization with the target population and its preferences, and it supported attribute/level refinement.

PMID: 25726011 [PubMed - as supplied by publisher]