Macular Degeneration Foundation™
Our focus is your vision

MD Research News

Issue 10

Monday Jan 10, 2010

This free weekly bulletin lists the latest published research articles on macular degeneration (MD) as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term “macular degeneration”.

If you have not already subscribed, please email Rob Cummins at **research@mdfoundation.com.au** with ‘Subscribe to MD Research News’ in the subject line, and your name and address in the body of the email.

You may unsubscribe at any time by an email to the above address with your ‘unsubscribe’ request.

Drug treatment

Retina. 2011 Jan;31(1):65-73.

COMBINATION THERAPY OF RANIBIZUMAB AND PHOTODYNAMIC THERAPY FOR RETINAL ANGIOMATOUS PROLIFERATION WITH SEROUS PIGMENT EPITHELIAL DETACHMENT IN KOREAN PATIENTS: Twelve-Month Results.

Lee MY, Kim KS, Lee WK.

From the Department of Ophthalmology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea.

PURPOSE: : The purpose of this study was to evaluate the safety and efficacy of combination therapy with intravitreal ranibizumab and photodynamic therapy in the treatment of retinal angiomatous proliferation (RAP) with serous pigment epithelial detachment.

METHODS: : Ten eyes of nine consecutive patients with newly diagnosed RAP were enrolled in this prospective pilot study. A course of combination therapy consisted of three ranibizumab injections at monthly intervals and a single photodynamic therapy, guided by indocyanine green angiography, about 1 week after the first injection. The patients were followed every month for 12 months. Retreatment was administered when a persistent, recurrent, or new RAP lesion was confirmed.

RESULTS: : Eight of the 9 patients (9 eyes) completed 12 months of follow-up. At the 3-month visit, 8 of the 9 eyes (89%) showed favorable initial responses. After 6 months, recurrent lesions developed in 2 eyes (25%) and a new lesion in one other eye; all showed favorable responses to retreatment. At the 12-month visit, 7 eyes (78%) showed regression of the RAP lesions, among which 5 eyes (56%) required only a single session of combination treatment. The mean best-corrected visual acuity was improved from 20/125 at baseline to 20/63 (P = 0.021), and the mean central foveal thickness was reduced from 353 μm at baseline to 169 μm (P = 0.017). The mean improvement in the best-corrected visual acuity was 3.86 lines. No patient had vision-threatening adverse events.

CONCLUSION: : Ranibizumab and photodynamic therapy combination therapy appears to be safe and effective for anatomical and functional improvement in patients with RAP with pigment epithelial detachment. Further evaluation with a larger patient sample and a long-term controlled study is required to compare treatment efficacy with antivascular endothelial growth factor monotreatment.

PMID: 21187732 [PubMed - in process]

Retina. 2011 Jan;31(1):31-5.

Bilateral intravitreal injection of antivascular endothelial growth factor therapy.

Mahajan VB, Elkins KA, Russell SR, Boldt HC, Gehrs KM, Weingeist TA, Stone EM, Abràmoff MD, Liu D, Folk JC.

From the *Vitreoretinal Service, Department of Ophthalmology and Visual Sciences, The University of Iowa Hospitals & Clinics, Iowa City, Iowa; †Omics Laboratory, Iowa City, Iowa; ‡Howard Hughes Medical Institute, Iowa City, IA; §VAMC, Iowa City, Iowa; and ¶Department of Biostatistics, University of Iowa, Iowa City, Iowa.

PURPOSE: : The purpose of this study was to review adverse events and patient preference after bilateral intravitreal injection of antibodies to vascular endothelial growth factor.

METHODS: : A retrospective case-control study. Patients with exudative age-related macular degeneration who received intravitreal antivascular endothelial growth factor agent injections in both eyes (bilateral group) on the same day over a 23-month period were compared with patients who received injections in only 1 eye. The occurrence of endophthalmitis, cerebrovascular accident, myocardial infarction, death, patient discomfort, and patient preference was compared between the two groups.

RESULTS: : One hundred and two patients received an average of 4.43 bilateral injections (range 1-13). A case-control group of 102 patients received an average of 10.2 unilateral injections, (range 2-28). Bevacizumab was injected 45.5%, ranibizumab 45.5%, and a combination of bevacizumab and ranibizumab 9% of the time for bilateral injections. Bevacizumab was used 50.3% and ranubizumab 49.7% of the time in unilateral injections. The follow-up of both groups averaged 18.4 months (range 4.7-36.5 months). There were no cases of endophthalmitis or cerebrovascular accident in either group. There was a single case of myocardial infarction in each group. There were two deaths in the bilateral group and three deaths in the unilateral group. More than 90% strongly preferred bilateral injections to unilateral injections.

CONCLUSION: : Bilateral injections of antivascular endothelial growth factor agents on the same day did not increase the rate of adverse events and was preferred by the majority of patients.

PMID: 21187731 [PubMed - in process]

Graefes Arch Clin Exp Ophthalmol. 2011 Jan 6. [Epub ahead of print]

The safety of using anti-VEGF: Is there strength in numbers? Curtis LH, Hammill BG, Schulman KA, Cousins SW (2010) Risks of mortality, myocardial infarction, bleeding, and stroke associated with therapies for age-related macular degeneration. Arch Ophthalmol 128(10):1273-1279.

Wong D, Joussen AM.

The Eye Institute, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, People's Republic of China, shdwong@hku.hk.

PMID: 21210141 [PubMed - as supplied by publisher]

Eur J Ophthalmol. 2010 Dec 9. pii: [Epub ahead of print]

Visual and optical coherence tomography outcomes of intravitreal bevacizumab and ranibizumab in inflammatory choroidal neovascularization secondary to punctate inner choroidopathy.

Spiteri Cornish K, Williams GJ, Gavin MP, Imrie FR.

Tennent Institute of Ophthalmology, Gartnavel General Hospital, Glasgow - UK.

Purpose. Choroidal neovascular membranes (CNV) are the major cause of visual loss in punctate inner choroidopathy (PIC), an idiopathic inflammatory condition predominantly affecting young, myopic women.

We present a case series of 9 patients with CNV associated with PIC, treated with intravitreal anti-vascular endothelial growth factor agents.

Methods. This is a retrospective case series of 9 patients treated with either intravitreal bevacizumab or ranibizumab for inflammatory CNV secondary to PIC. Initial and posttreatment converted logMAR visual acuity, fundus fluorescein angiograms (FFA), optical coherence tomography (OCT), previous and concurrent treatments, and side effects were recorded. Informed consent for treatment was obtained from each patient.

Results. Nine patients (8 female, 1 male) with an average age of 34.4 years were treated for an average of 14.9 months. Six patients were treated with bevacizumab, and 3 with ranibizumab, with a mean of 2.34 injections per year. The mean visual acuity gain for the whole group of 9 patients was 0.26 converted logMAR units (Wilcoxon signed-rank test, $p<0.015$). Eight patients remained stable or had visual improvement at final follow-up, with a mean gain of 0.36 converted logMAR units. Only one patient's vision deteriorated (loss of 0.48 converted logMAR units). Concomitant short courses of oral corticosteroid were used in 3 of the 9 patients.

Conclusions. Over a 1-year period, bevacizumab and ranibizumab can be safely and successfully used to treat inflammatory CNV secondary to PIC, avoiding the need for systemic immunosuppression in the majority of patients.

PMID: 21188681 [PubMed - as supplied by publisher]

Other treatment & diagnosis

J Biomed Opt. 2010 November/December;15(6):061704.

Segmentation and quantification of retinal lesions in age-related macular degeneration using polarization-sensitive optical coherence tomography.

Baumann B, Götzinger E, Pircher M, Sattmann H, Schütze C, Schlanitz F, Ahlers C, Schmidt-Erfurth U, Hitzenberger CK.

Medical University of Vienna, Center for Medical Physics and Biomedical Engineering, Währinger Straße 13, A-1090 Vienna, Austria.

Abstract

We present polarization-sensitive optical coherence tomography (PS-OCT) for quantitative assessment of retinal pathologies in age-related macular degeneration (AMD). On the basis of the polarization scrambling characteristics of the retinal pigment epithelium, novel segmentation algorithms were developed that allow one to segment pathologic features such as drusen and atrophic zones in dry AMD as well as to determine their dimensions. Results from measurements in the eyes of AMD patients prove the ability of PS-OCT for quantitative imaging based on the retinal features polarizing properties. Repeatability measurements were performed in retinas diagnosed with drusen and geographic atrophy in order to evaluate the performance of the described methods. PS-OCT appears as a promising imaging modality for three-dimensional retinal imaging and ranging with additional contrast based on the structures' tissue-inherent polarization properties.

PMID: 21198152 [PubMed - as supplied by publisher]

J Biomed Opt. 2010 Nov-Dec;15(6):061714.

Simple and objective method for routine detection of the macular pigment xanthophyll.

Schweitzer D, Jentsch S, Dawczynski J, Hammer M, Wolf-Schnurrbusch UE, Wolf S.

Augenklinik der Friedrich-Schiller-Universität Jena, Experimentelle Ophthalmologie Bachstrasse 18 07743 Jena, Germany.

Abstract

A new simple method for two-dimensional determination of optical density of macular pigment xanthophyll (ODx) in clinical routine is based on a single blue-reflection fundus image. Individual different vignetting is corrected by a shading function. For its construction, nodes are automatically found in structureless image regions. The influence of stray light in elderly crystalline lenses is compensated by a correction function that depends on age. The reproducibility of parameters in a one-wavelength reflection method determined for three subjects (47, 61, and 78 years old) was: maxODx = 6.3%, meanODx = 4.6%, volume = 6%, and area = 6% already before stray-light correction. ODx was comparable in pseudophakic and in an eye with a crystalline lens of the same 11 subjects after stray-light correction. Significant correlation in ODx was found between the one-wavelength reflection method and the two-wavelength autofluorescence method for pseudophakic and cataract eyes of 19 patients suffering from dry age-related macular degeneration (AMD) (R(2) = 0.855). In pseudophakic eyes, maxODx was significantly lower for dry AMD (n = 45) (ODx = 0.491±0.102 ODU) than in eyes with healthy fundus (n = 22) (ODx = 0.615±0.103 ODU) (p = 0.000033). Also in eyes with crystalline lens, maxODx was lower in AMD (n = 125) (ODx = 0.610±0.093 ODU) than in healthy subjects (n = 45) (ODx = 0.674±0.098 ODU) (p = 0.00019). No dependence on age was found in the pseudophakic eyes both of healthy subjects and AMD patients.

PMID: 21198162 [PubMed - in process]

Value Health. 2011 Jan;14(1):110-20.

Metric properties of the MacDQoL, individualized macular-disease-specific quality of life instrument, and newly identified subscales in French, German, Italian, and American populations.

Berdeaux G, Mesbah M, Bradley C.

Alcon, Rueil-Malmaison, France; Conservatoire National des Arts et Métiers, Paris, France.

Abstract

OBJECTIVES: The aims of this analysis were to confirm the UK results in other countries and to explore the possibility of subscales of the 25-Item Macular disease Dependent Quality of Life (MacDQoL) questionnaire.

METHODS: Two clinical studies were pooled. Principal components analyses (Varimax) were conducted on baseline data from each country and from all combined. Factorial structures were compared between countries, and Cronbach alpha values were used to identify item clusters. Four groups of patients were created according to visual acuity (VA) in the best eye (BE <10/20; BE ≥10/20) and worst eye (WE <10/100; WE ≥10/100). These groups were used to investigate (analysis of variance) the sensitivity of MacDQoL to VA impairment and to compare it with the NEI-VFQ-25 generic visual function questionnaire.

RESULTS: A total of 797 patients (mean age 76.8 years; 55.8% women) had wet age-related macular degeneration (AMD). Strong correlations between the MacDQoL items (r > 0.48) and factor loadings >0.49 on a forced one-factor analysis supported the use of an average weighted impact score. Four constructs (Cronbach alpha >0.8) were derived, represented by the labels: Essential tasks, Family/social life, Activities/capabilities, and Embarrassment. The structure did not differ among the four countries involved, except one item (Finance), which has been excluded. Patients with BE VA <10/20 and WE VA <10/100 produced significantly worse overall scores than those with BE VA >10/20 and WE VA >10/100 (MacDQoL P < 0.0001; NEI-VFQ-25 P < 0.0001).

CONCLUSIONS: The analysis confirmed the metric properties of the MacDQoL. The MacDQoL offers a broad individualized measure of the impact of MD on quality of life.

PMID: 21211493 [PubMed - in process]

J Laryngol Otol. 2010 Dec 16:1-5. [Epub ahead of print]

Association of age-related macular degeneration with age-related hearing loss.

Bozkurt MK, Ozturk BT, Kerimoglu H, Ersan I, Arbag H, Bozkurt B.

Department of Otolaryngology, Meram Medical Faculty, Selcuk University, Konya, Turkey.

Objective: To assess the association between age-related macular degeneration and age-related hearing loss in Turkish subjects aged 50 years or older.

Study design and setting:Prospective, case control study within a tertiary university hospital.

Subjects and methods: Fifty subjects with age-related macular degeneration and 43 healthy subjects underwent ophthalmological and otolaryngological examination. Statistical analyses were conducted for the poorer eye and ear, comparing age-related hearing loss and pure tone average in the macular degeneration group versus controls.

Results: Median pure tone average was significantly poorer in the macular degeneration group (35 dBHL) compared with controls (23 dBHL). In the macular degeneration group, hearing loss was significantly greater in dry type (43 dBHL) than wet type (32 dBHL) cases. There was a significant difference between the prevalence of varying degrees of hearing loss in the macular degeneration versus control groups, being respectively: mild, 50 and 35 per cent; moderate, 20 and 5 per cent; and severe, 6 and 0 per cent. There was a weak, but significant correlation between each patient's visual acuity and pure tone average results (rsÂ =Â â 0.37, pÂ <Â 0.001).

Conclusion: Age-related hearing loss is more common in patients with age-related macular degeneration. Such patients should be questioned regarding hearing difficulty, and referred to an otolaryngologist if appropriate.

PMID: 21205373 [PubMed - as supplied by publisher]

Genetics

Hum Mol Genet. 2010 Dec 31. [Epub ahead of print]

The Na/K-ATPase is obligatory for membrane anchorage of retinoschisin, the protein involved in the pathogenesis of X-linked juvenile retinoschisis.

Friedrich U, Stöhr H, Hilfinger D, Loenhardt T, Schachner M, Langmann T, Weber BH.

Institute of Human Genetics, University of Regensburg, Franz-Josef-Strauss-Allee 11, 93053 Regensburg, Germany.

Abstract

Mutations in the RS1 gene encoding the discoidin-domain containing retinoschisin cause X-linked juvenile retinoschisis (XLRS), a common macular degeneration in males. Disorganization of retinal layers and ERG abnormalities are hallmarks of the disease and are also found in mice deficient for the orthologous murine protein, indicating that retinoschisin is important for the maintenance of retinal cell integrity. Upon secretion, retinoschisin associates with plasma membranes of photoreceptor and bipolar cells although the components by which the protein is linked to membranes in vivo are still unclear. Here, we show that retinoschisin fails to bind to phospholipids or unilamellar lipid vesicles. A recent proteomic approach identified the Na/K-ATPase subunits ATP1A3 and ATP1B2 as binding partners of retinoschisin. We analyzed mice deficient for retinoschisin (Rs1h(-/Y)) and ATP1B2 (Atp1b2(-/-)) to characterize the role of Na/K-ATPase interaction in the organization of retinoschisin on cellular membranes. We demonstrate that both the Na/K-ATPase and retinoschisin are significantly reduced in Atp1b2(-/-)retinas suggesting that retinoschisin membrane association is severely impaired in the absence of ATP1A3 and ATP1B2 subunits. Conversely, the presence of ATP1A3 and ATP1B2 are obligatory for binding of exogenously applied

retinoschisin to crude membranes. Also, co-expression of ATP1A3 and ATP1B2 is required for retinoschisin binding to intact Hek293 cells. Taken together, our data support a predominant role of Na/K-ATPase in anchoring retinoschisin to retinal cell surfaces. Furthermore, altered localization of ATP1A3 and ATP1B2 is a notable consequence of retinoschisin deficiency and thus may be an important downstream aspect of cellular pathology in XLRS.

PMID: 21196491 [PubMed - as supplied by publisher]

Mol Vis. 2010 Dec 17;16:2811-21.

Genome-wide association analyses of genetic, phenotypic, and environmental risks in the age-related eye disease study.

Ryu E, Fridley BL, Tosakulwong N, Bailey KR, Edwards AO.

PURPOSE: To present genome-wide association analyses of genotypic and environmental risks on age-related macular degeneration (AMD) using 593 subjects from the age-related eye disease study (AREDS), after adjusting for population stratification and including questionable controls.

METHODS: Single nucleotide polymorphism (SNP) associations with AMD for the non-Hispanic white population were investigated using a log-additive model after adjusting for population stratification. Replication of possible SNP-disease association was performed by genotyping an independent group of 444 AMD case and 300 control subjects. Logistic regression models were used to assess interaction effects between smoking and SNPs associated with AMD. Independent genetic risk effects among the disease-associated SNPs were also investigated using multiple logistic regression models.

RESULTS: Population stratification was observed among the individuals having a self-reported race of non-Hispanic white. Risk allele frequencies at established AMD loci demonstrated that questionable control subjects were similar to control subjects in the AREDS, suggesting that they could be used as true controls in the analyses. Genetic loci (complement factor H [CFH], complement factor B [CFB], the age-related maculopathy susceptibility 2 locus containing the hypothetical gene [LOC387715]/the high-temperature requirement A-1 [HTRA1], and complement component 3 [C3]) that were already known to be associated with AMD were identified. An additional 26 novel SNPs potentially associated with AMD were identified, but none were definitely replicated in a second independent group of subjects. Smoking did not interact with known AMD loci, but was associated with late AMD. Statistically independent genetic signals were observed within the Pleckstrin homology domain-containing family A member 1 (PLEKHA1) region near LOC387715/HTRA1 and within a haplotype spanning exon 19 of the C3 gene.

CONCLUSIONS: Population stratification among Caucasian subjects from the multicentered AREDS was observed, suggesting that it should be adjusted for in future studies. The AREDS questionable control subjects can be used as control subjects in the AREDS genome-wide association study (GWAS). Smoking was an independent risk factor for advanced AMD in the AREDS subjects. There continues to be evidence that the 10q26 (age-related maculopathy susceptibility 2 gene [ARMS2]) locus spanning PLEKHA1-LOC387715-HTRA1 and the C3 gene may contain multiple independent genetic risks contributing to AMD.

PMID: 21197116 [PubMed - in process]PMCID: PMC3008720

Ophthalmic Res. 2011 Jan 5;46(1):31-37. [Epub ahead of print]

Glutathione S-Transferase M1, GSTT1 and GSTP1 Genetic Polymorphisms and the Risk of Age-Related Macular Degeneration.

Güven M, Görgün E, Unal M, Yenerel M, Batar B, Küçümen B, Dinç UA, Güven GS, Ulus T, Yüksel A.

Department of Medical Biology, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, Turkey.

Purpose: To determine the possible effects of glutathione S-transferase (GST) M1, GSTT1 and GSTP1 genetic polymorphisms on the risk of developing age-related macular degeneration (AMD).

Patients and Methods: This case-control study included a total of 120 patients with AMD (65 with dry-type AMD and 55 with wet-type AMD) and 198 disease-free controls. GSTM1 and GSTT1 polymorphisms were analyzed by using a multiplex polymerase chain reaction (PCR), and GSTP1 polymorphism was detected by real-time PCR assay.

Results:GSTM1-null genotype was significantly associated with the development of AMD (p = 0.01, OR = 1.82, 95% CI = 1.14-2.91). Stratification by AMD subtypes revealed a significant relationship between GSTM1-null genotype and dry-type AMD (p = 0.02, OR = 1.98, 95% CI = 1.10-3.53). In a stepwise regression model, only GSTM1-null genotype was significantly associated with the development of AMD (p = 0.01, OR = 1.77, 95% CI = 1.11-2.81).

Conclusions: Our findings suggest that genetic polymorphisms of GST may have a role in the development of AMD.

PMID: 21212706 [PubMed - as supplied by publisher]

Mol Vis. 2010 Dec 31;16:2923-30.

Elevated C-reactive protein levels and ARMS2/HTRA1 gene variants in subjects without age-related macular degeneration.

Yasuma TR, Nakamura M, Nishiguchi KM, Kikuchi M, Kaneko H, Niwa T, Hamajima N, Terasaki H.

PURPOSE: To investigate the association between the serum high sensitivity C-reactive protein (hs-CRP) levels and variants in age-related maculopathy susceptibility 2 (ARMS2)/HtrA serine peptidase 1 (HTRA1) genes in normal subjects with no evidence of age-related macular degeneration (AMD).

METHODS: After clinical evaluation, information related to medical and social history was collected from 476 Japanese individuals (age range 17-89 years) along with blood samples. These subjects were medical checkup participants recruited at Nagoya University Hospital with no macular disease, as confirmed by fundus photographs. Serum hs-CRP levels were measured using a highly sensitive latex aggregation immunoassay. The genotypes of three polymorphisms in the ARMS2/HTRA1 locus, i.e., *372_815del443ins54 (del/ins), rs10490924, and rs11200638 were determined using direct sequencing and/or PCR-based assays. After the haplotype was constructed and analyzed, the associations between hs-CRP levels and representative del/ins genotypes were studied with and without adjustment for potential confounding factors.

RESULTS: All three polymorphisms in the ARMS2/HTRA1 region were in almost complete linkage disequilibrium. Haplotype analyses showed the existence of only two common haplotypes, together comprising 98.9%. Regression analyses showed that the level of hs-CRP was positively correlated with increasing age. This age-dependent increase of hs-CRP levels was greatest in those with homozygous del/ins alleles and lowest in those with homozygous wild-type alleles, which was significant assuming an additive model for gene-dosage association (univariate analyses: p=0.016, multivariate analyses including smoking status, past medical history, and BMI: p=0.043). Consequently, the level of hs-CRP was greatest in those with homozygous del/ins alleles and lowest in those with homozygous wild-type alleles when subjects older than 60 were analyzed. This was significant assuming an additive model for gene-dosage association (univariate analyses: p=0.032).

CONCLUSIONS: An age-dependent elevation of serum hs-CRP levels may be accelerated in normal subjects with one or two risk alleles in the ARMS2/HTRA1 locus compared to those with homozygous wild-type alleles. The results of the current study show that the as-yet undetermined function of variants in the ARMS2/HTRA1 locus might be linked to inflammation, possibly contributing to the development of neovascular AMD.

PMID: 21203342 [PubMed - in process]PMCID: PMC3013066

Pathogenesis & epidemiology

Front Biosci. 2011 Jan 1;16:1291-301.

DNA damage and repair in age-related macular degeneration.

Blasiak J, Szaflik JP.

Department of Molecular Genetics, University of Lodz, Banacha 12/16, 90-237 Lodz, Poland.

Abstract

Oxidative stress may play an important role in the pathogenesis of age-related macular degeneration (AMD). Mitochondria produce reactive oxygen species (ROS), which induce degenerative changes typical for AMD. Mitochondrial DNA (mtDNA) is targeted by ROS and it is considered to be more vulnerable to damage than nuclear DNA (nDNA) due to the impaired DNA repair system, lack of nucleosomal organization and close vicinity of mitochondrial oxidative chain. Some reports suggest the association between mtDNA damage and AMD. However, the metabolism of mtDNA is mainly determined by the expression of nDNA. Therefore, the extent of damage to mtDNA in retinal cells depends on the overall efficacy of nDNA repair, which decreases with age. We showed an association between nDNA damage and repair and AMD. Also well-recognized factors of AMD pathogenesis, age and smoking, may exert their effects through the DNA damage and repair. In conclusion, DNA damage and repair, both in mitochondrial and nuclear genome, may play an important role in the pathogenesis of AMD, and their mutual relationship in this disease needs further study.

PMID: 21196232 [PubMed - in process]

Front Biosci. 2011 Jan 1;16:1551-9.

Implications of altered iron homeostasis for age-related macular degeneration.

Blasiak J, Szaflik J, Szaflik JP.

Department of Molecular Genetics, University of Lodz, Banacha 12/16, 90-237 Lodz, Poland.

Abstract

Reactive oxygen species (ROS) may contribute to the pathogenesis of age-related macular degeneration (AMD) and they can be produced in the Fenton reaction catalyzed by Fe3+ ions. Therefore, altered homeostasis of iron in the retina may be the source of ROS and its damage resulting in clinically detectable AMD symptoms. The results of some post mortem research indicate a higher concentration of iron in AMD retinas in comparison with non-affected retinas, although those results do not determine whether iron overload is the reason or a consequence of AMD. However, the results of some other research suggest that iron may contribute to the pathogenesis of AMD. Those include increasing of macular iron level with age, involvement of iron in the pathogenesis of some degenerative diseases linked with AMD, upregulation of transferrin in AMD, developing of AMD-like syndromes in mice deficient in ceruloplasmin and hephaestin, association between polymorphism of the iron homeostasis genes and AMD and others. Better understanding of the role of altered iron homeostasis may be useful in prevention and curing of AMD.

Ophthalmology. 2011 Jan 4. [Epub ahead of print]

Choroidal Thickness in Polypoidal Choroidal Vasculopathy and Exudative Age-Related Macular Degeneration.

Chung SE, Kang SW, Lee JH, Kim YT.

Abstract

PURPOSE: To compare choroidal thickness between eyes with polypoidal choroidal vasculopathy (PCV) and eyes with age-related macular degeneration (AMD).

DESIGN: Observational, comparative case series.

PARTICIPANTS: Twenty-five eyes with PCV, 14 uninvolved fellow eyes with PCV, 30 eyes with exudative AMD, 17 eyes with early AMD, and 20 eyes of age-matched normal subjects.

METHODS: Choroidal thickness was measured using enhanced-depth imaging optical coherence tomography. Subfoveal choroidal thickness in each eye was analyzed by measurement of the vertical distance from the Bruch's membrane to the innermost scleral layer. Nasal, superior, temporal, and inferior choroidal thicknesses, 1500 μm apart from the foveal center, were also evaluated in all eyes.

MAIN OUTCOME MEASURES: Choroidal thickness in each group.

RESULTS: Mean (± standard deviation) subfoveal choroidal thickness in eyes with PCV and in their uninvolved fellow eyes was 438.3±87.8 μm and 372.9±112.0 μm, respectively, which was significantly greater than in eyes of age-matched normal subjects (224.8±52.9 μm) ($P<0.001$ and $P = 0.003$, respectively). Subfoveal choroidal thickness of eyes with exudative AMD (171.2±38.5 μm) and eyes with early AMD (177.4±49.7 μm) was thinner than that of age-matched normal subjects ($P = 0.004$ and $P = 0.078$, respectively). Choroidal thickness at each of the other 4 points showed a similar tendency.

CONCLUSIONS: This study demonstrates thickening of choroid in the eyes with PCV, in contrast with choroidal thinning observed in eyes with AMD. These findings suggest involvement of different pathogenic mechanisms in PCV from those in exudative AMD.

PMID: 21211846 [PubMed - as supplied by publisher]

Pre-clinical

Aging (Albany NY). 2010 Dec 12. [Epub ahead of print]

Alterations of retinal pigment epithelium cause AMD-like retinopathy in senescence-accelerated OXYS rats.

Markovets AM, Saprunova VB, Zhdankina AA, Fursova AZ, Bakeeva LE, Kolosova NG.

Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia.

Abstract

Pathogenesis of age-related macular degeneration (AMD), the leading cause of blindness in the world, remains poorly understood. This makes it necessary to create animal models for studying AMD pathogenesis and to design new therapeutic approaches. Here we showed that retinopathy in OXYS rats is similar to human AMD according to clinical signs, morphology, and vascular endothelium growth factor (VEGF) and pigment epithelium-derived factor (PEDF) genes expression. Clinical signs of retinopathy OXYS rats manifest by the age 3 months against the background of significantly reduced expression level of VEGF and PEDF genes due to the decline of the amount of retinal pigment epithelium (RPE) cells and alteration of choroidal microcirculation. The disruption in OXYS rats' retina starts at the age of 20 days and appears as reduce the area of RPE cells but does not affect their ultrastructure. Ultrastructural pathological alterations of RPE as well as develop forms of retinopathy are observed in OXYS rats from age 12 months and manifested as excessive accumulation of lipofuscin in RPE regions adjacent to the rod cells, whirling extentions of the basement membrane into the cytoplasm. These data suggest that primary cellular degenerative alterations in the RPE cells secondarily lead to choriocapillaris atrophy and results in complete loss of photoreceptor cells in the OXYS rats' retina by the age of 24 months.

PMID: 21191149 [PubMed - as supplied by publisher]

PLoS One. 2010 Dec 30;5(12):e15730.

The Tight Junction Associated Signalling Proteins ZO-1 and ZONAB Regulate Retinal Pigment Epithelium Homeostasis in Mice.

Georgiadis A, Tschernutter M, Bainbridge JW, Balaggan KS, Mowat F, West EL, Munro PM, Thrasher AJ, Matter K, Balda MS, Ali RR.

Department of Genetics, UCL Institute of Ophthalmology, University College London, London, United Kingdom.

Abstract

Cell-cell adhesion regulates the development and function of epithelia by providing mechanical support and by guiding cell proliferation and differentiation. The tight junction (TJ) protein zonula occludens (ZO)-1 regulates cell proliferation and gene expression by inhibiting the activity of the Y-box transcription factor ZONAB in cultured epithelial cells. We investigated the role of this TJ-associated signalling pathway in the retinal pigment epithelium (RPE) in vivo by lentivirally-mediated overexpression of ZONAB, and knockdown of its cellular inhibitor ZO-1. Both overexpression of ZONAB or knockdown of ZO-1 resulted in increased RPE proliferation, and induced ultrastructural changes of an epithelial-mesenchymal transition (EMT)-like phenotype. Electron microscopy analysis revealed that transduced RPE monolayers were disorganised with increased pyknosis and monolayer breaks, correlating with increased expression of several EMT markers. Moreover, fluorescein angiography analysis demonstrated that the increased proliferation and EMT-like phenotype induced by overexpression of ZONAB or downregulation of ZO-1 resulted in RPE dysfunction. These findings demonstrate that ZO-1 and ZONAB are critical for differentiation and homeostasis of the RPE monolayer and may be involved in RPE disorders such as proliferative vitroretinopathy and atrophic age-related macular degeneration.

PMID: 21209887 [PubMed - in process]

Curr Neurovasc Res. 2011 Jan 5. [Epub ahead of print]

An Arylidene-Thiazolidinedione Derivative, GPU-4, without PPARγ Activation, Reduces Retinal Neovascularization.

Nakamura S, Hayashi K, Takizawa H, Murase T, Tsuruma K, Shimazawa M, Kakuta H, Nagasawa H, Hara H.

Molecular Pharmacology, Department of Biofunctional Evaluation, Gifu Pharmaceutical University, Gifu, Japan. hidehara@gifu-pu.ac.jp.

Retinal angiogenesis is a leading cause of blindness, including retinopathy of prematurity, diabetic retinopathy, and age-related macular degeneration. Vascular endothelial growth factor (VEGF) is one of the major angiogenesis factors, and induces endothelial cell proliferation and migration. VEGF stimulates NADPH oxidase to produce reactive oxygen species (ROS), and ROS induce the transcription factors and genes involved in angiogenesis. In the present study, we demonstrated that GPU-4, 5-arylidene-2,4-thiazolidinedione derivative, demonstrates anti-angiogenic activity regarding human retinal microvascular endothelial cells (HRMECs) and retinal neovascularization in a mouse model of retinopathy of prematurity. GPU-4 inhibited the VEGF-induced radicals, proliferation, and migration in HRMECs without a PPARγ-mediated effect. Furthermore, systemic administration of GPU-4 inhibited the development of retinal neovascularization in a murine oxygen-induced retinopathy model but did not exert revascularization of the capillary-free area, which shows normal physiological revascularization. These findings indicate that GPU-4 suppressed in vitro and in vivo retinal neovascularization partly by a radical scavenging effect, suggesting that GPU-4 might be a potential therapeutic agent candidate for proliferative diseases of the retinal vasculature.

PMID: 21208163 [PubMed - as supplied by publisher]