Macular Degeneration Foundation
Our focus is your vision

MD Research News

Issue 30

Monday May 30 , 2011

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

Clin Ophthalmol. 2011;5:567-72. Epub 2011 May 6.

Electrophysiologic changes after intravitreal ranibizumab injection for the treatment of choroidal neovascular membrane (CNVM).

Bhurayanontachai P, Ratanasukon M, Jirarattanasopa P.

Retina Unit, Department of Ophthalmology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand.

PURPOSE: To determine the pattern of electroretinographic change after an intravitreal ranibizumab (Lucentis(®)) injection for the treatment of choroidal neovascular membrane (CNVM).

PATIENTS AND METHODS: A prospective interventional case series of patients treated by intravitreal ranibizumab injection. Best corrected visual acuity, optical coherence tomography (OCT), and multifocal electroretinography (mfERG) were assessed prior to treatment, and 2 weeks, 1 and 3 months after treatment. Primary outcome was the functional change in amplitude and implicit time by mfERG and secondary outcome was the structural change in macular thickness by optical coherence tomography (OCT).

RESULTS: Twenty-six eyes from 25 consecutive patients were enrolled. At 3 months after treatment, the mean visual acuity (VA) improved from 1.06 to 0.84 logMAR (P = 0.034) and the mean macular thickness decreased from 389.7 to 264.4 microns (P = 0.003). The mean implicit time of the central zone showed an improvement at 3 months after treatment when compared with the response at baseline (P = 0.024) and at 1 month (P = 0.013) but the mean amplitude showed no significant change. In subgroup analysis, the eyes with initial visual acuity (VA) ≥ 20/200 had a significant improvement in mean implicit time of the peripheral zone at 2 weeks after treatment (P = 0.028). The OCT revealed a significant decrease (P < 0.003) in macular thickness at 1 and 3 months postoperatively.

CONCLUSION: The mean implicit time of the central zone improved significantly at 3 months after treatment, whereas the mean amplitude showed no significant change. The macular thickness decreased significantly after the treatment, while VA improved to a lesser extent.

PMID: 21607026 [PubMed - in process]

PMCID: PMC3096619

Retina. 2011 May 20. [Epub ahead of print]

ASSOCIATION BETWEEN FOVEAL MICROSTRUCTURE AND VISUAL OUTCOME IN AGE-RELATED MACULAR DEGENERATION.

Shin HJ, Chung H, Kim HC.

From the Department of Ophthalmology, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, Republic of Korea.

PURPOSE: To investigate the correlation between foveal photoreceptor integrity and final visual acuity after treatment of eyes with neovascular age-related macular degeneration, and to determine the visual prognostic factors.

METHODS: We retrospectively studied 40 eyes of 40 patients with neovascular age-related macular degeneration who were treated successfully with intravitreal anti-vascular endothelial growth factor injection. Using spectral-domain optical coherence tomography, the eyes were categorized into three groups at the final visit, the V group with a completely visible photoreceptor inner and outer segment junction (IS/OS), the P group with a partially detected IS/OS, and the I group with an invisible IS/OS. The length of disrupted IS/OS and external limiting membrane, central macular thickness, and choroidal neovascularization size at the initial and final visits were measured. Retinal pigment epithelium regularity and outer nuclear layer thickness at the final visit were also evaluated.

RESULTS: Final visual acuity was closely associated with IS/OS integrity at the final visit. Final visual acuity (logarithm of minimum angle of resolution) in the V group (0.13 ± 0.10) was better than that in the P group (0.41 ± 0.31), and final visual acuity in the P group was better than that in the I group (0.97 ± 0.51) ($P < 0.001$). Shorter disrupted IS/OS and external limiting membrane length at the final visit were closely associated with better final visual acuity. Preservation of the IS/OS and external limiting membrane, thinner central macular thickness, and shorter choroidal neovascularization height before treatment were associated with intact photoreceptor integrity after resolution of exudation. However, central macular thickness, outer nuclear layer thickness, and retinal pigment epithelium regularity at the final visit had no significant correlation with photoreceptor integrity.

CONCLUSION: Foveal photoreceptor integrity was closely associated with final visual acuity in neovascular age-related macular degeneration after treatment. Initial visual acuity, IS/OS and external limiting membrane integrity, central macular thickness, and choroidal neovascularization height were correlated with final photoreceptor integrity, and they wound be visual prognostic factors after resolution of exudation.

PMID: 21606888 [PubMed - as supplied by publisher]

Semin Ophthalmol. 2011 May;26(3):69-76.

Bevacizumab and neovascular age related macular degeneration: pathogenesis and treatment.

El-Mollayess GM, Noureddine BN, Bashshur ZF.

The Department of Ophthalmology, American University of Beirut, Beirut, Lebanon.

Abstract

The pathogenesis of neovascular age related macular degeneration (AMD) is multifactorial including inflammation and angiogenesis leading to choroidal neovascularization (CNV). Therapy against vascular endothelial growth factor (VEGF) has revolutionized the treatment of neovascular AMD. Intravitreal off-label use of bevacizumab proved to be safe. This literature review was conducted to study improvement in visual acuity, change in central retinal thickness (CRT), safety, pharmacodynamics, and possible resistance to intravitreal bevacizumab over a one-year period in eyes with neovascular AMD. We reviewed articles be-

tween 1997 and January 2010 that included at least 30 patients with AMD who received intravitreal bevacizumab monotherapy for at least 1 year. The mean number of letters gained, decrease in CRT, and number of injections were 8 letters, 125.3 µm, and 4.3 injections, respectively. Further, randomized prospective clinical trials are needed to determine the efficacy and safety of intravitreal bevacizumab in the treatment of neovascular AMD.

PMID: 21609219 [PubMed - in process]

Semin Ophthalmol. 2011 May;26(3):114-20.

Review of combination therapies for neovascular age-related macular degeneration.

Couch SM, Bakri SJ.

Mayo Clinic, Department of Ophthalmology, Rochester, MN, USA.

Abstract

While angiogenesis is one of the factors associated with the development of CNV due to age-related macular degeneration (AMD), inflammation and oxidative stress also appear to play a role. Treatment of CNV with intravitreal anti-vascular endothelial growth factor monotherapy is currently the standard of care. However, not all patients respond to monotherapy, and combination therapy may target the CNV through multiple mechanisms, thus reducing treatment frequency or improving visual outcome. Photodynamic therapy (with regular or reduced fluence), as well as intravitreal steroids are used in combination with anti-VEGF therapy. This paper reviews the many clinical trials that have been performed utilizing several combinations of double and triple therapy. While combination therapy is biologically justifiable, further study is required to determine correct combinations and dosage.

PMID: 21609223 [PubMed - in process]

Semin Ophthalmol. 2011 May;26(3):149-55.

Emerging therapies for the treatment of neovascular age related macular degeneration.

Yuan A, Kaiser PK.

Cole Eye Institute, Cleveland, OH, USA.

Abstract

Numerous drugs that show promise in the treatment of neovascular age related macular degeneration are currently being evaluated in early clinical trials. Some of these drugs target the vascular endothelial growth factor pathway while others act on different targets along the angiogenesis cascade. The mechanism of action of these novel therapeutics and the results of early clinical trials will be discussed along with a review of angiogenesis.

PMID: 21609228 [PubMed - in process]

Semin Ophthalmol. 2011 May;26(3):139-48.

Endophthalmitis following intravitreal anti-vascular endothelial growth factor injections for neovascular age-related macular degeneration.

Moshfeghi AA.

Bascom Palmer Eye Institute, Department of Ophthalmology, University of Miami Miller School of Medicine, Palm Beach Gardens, FL, USA.

Abstract

Endophthalmitis following intravitreal injections of therapeutic medications is a rare but potentially vision-threatening problem. Infectious agents associated with endophthalmitis following injection of vascular endothelial growth factor (VEGF) inhibitors are typically Gram positive organisms with a predominance of Streptococcal and Staphylococcal microbiologic isolates. Patients with infectious endophthalmitis generally present within the first 72 hours following an intravitreal anti-VEGF injection with complaints of pain, redness, and decreased vision. Prompt treatment with a conventional endophthalmitis management approach may mitigate irreversible vision loss; however, poorer outcomes have been reported with more virulent organisms such as those associated with Streptococcal species. As the number of intravitreal injections performed each year continues to increase, ophthalmologists must maintain a rigorous approach to their injection technique and remain vigilant for the signs and symptoms of endophthalmitis.

PMID: 21609227 [PubMed - in process]

Int Ophthalmol. 2011 May 25. [Epub ahead of print]

Sustained ocular hypertension following intravitreal injections of 0.5 mg/0.05 ml ranibizumab.

Loukianou E, Brouzas D, Apostolopoulos M.

Moorfields Eye Hospital, 25A Bavaria Road, Islington, N19 4EU, London, UK, eleniloukianou@yahoo.com.

Abstract: To report three cases with sustained ocular hypertension following intravitreal injections of 0.5 mg/0.05 ml ranibizumab and to underline the importance of monitoring intraocular pressure (IOP) following intravitreal injections of ranibizumab (Lucentis). Three patients were found to have high IOP after intravitreal injections of 0.5 mg/0.05 ml ranibizumab. IOP was elevated after the second ranibizumab injection in patients 1 and 2, and after the third injection in patient 3. The increase in IOP was sustained, requiring treatment with anti-glaucoma eye drops in all patients, the addition of systemic carbonic anhydrase inhibitor in one patient, and the application of selective laser trabeculoplasty (SLT) in another patient. None of the patients had a previous history of glaucoma or ocular hypertension. Sustained ocular hypertension may occur after intravitreal injections of 0.5 mg/0.05 ml ranibizumab. Although the precise mechanism of the pressure rise is unknown, three eyes in our series were controlled with topical or oral medication and one with SLT. The necessity of IOP monitoring is strongly emphasized after intravitreal injections of 0.5 mg/0.05 ml ranibizumab.

PMID: 21611879 [PubMed - as supplied by publisher]

Retina. 2011 May 23. [Epub ahead of print]

INTRAVITREAL RANIBIZUMAB WITH OR WITHOUT PHOTODYNAMIC THERAPY FOR THE TREATMENT OF SYMPTOMATIC POLYPOIDAL CHOROIDAL VASCULOPATHY.

Lai TY, Lee GK, Luk FO, Lam DS.

From the Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Kowloon. Hong Kong.

PURPOSE: To evaluate the efficacy of intravitreal ranibizumab with or without verteporfin photodynamic therapy (PDT) in the treatment of symptomatic polypoidal choroidal vasculopathy.

METHODS: Twenty-three eyes of 23 patients received 3 monthly intravitreal ranibizumab injections with or

without indocyanine green angiography-guided PDT at baseline. All patients had follow-up of ≥12 months. Visual and anatomical outcomes were compared between the two groups and a PDT monotherapy group.

RESULTS: Seven eyes had ranibizumab monotherapy, 16 had combined ranibizumab injections and verteporfin PDT, and 12 had PDT monotherapy. At 3 months, the mean logarithm of minimal angle of resolution best-corrected visual acuity improved from 0.92 to 0.74 in the ranibizumab group (P = 0.18), from 0.70 to 0.59 in the combined group (P = 0.037), and from 0.74 to 0.57 in the PDT monotherapy group (P = 0.014). Complete regression of polypoidal lesions in indocyanine green angiography was found in 1 (14.3%) eye in the ranibizumab group, compared with 15 (93.8%) eyes in the combined group (P = 0.001). Additional PDT and ranibizumab injections in eyes with persistent polyps and fluorescein leakage resulted in regression of polyps in all eyes. At 12 months, no significant difference in logarithm of minimal angle of resolution best-corrected visual acuity and visual change was found between eyes initially treated with ranibizumab monotherapy, combined ranibizumab and PDT, or PDT monotherapy (P = 1.00 and P = 0.11, respectively).

CONCLUSION: Intravitreal ranibizumab appeared to result in stabilization of vision in patients with symptomatic polypoidal choroidal vasculopathy. However, combined ranibizumab and PDT appeared to be more effective in causing complete regression of the polypoidal lesions in indocyanine green angiography compared with ranibizumab monotherapy.

PMID: 21610566 [PubMed - as supplied by publisher]

Isr Med Assoc J. 2011 Mar;13(3):141-6.

National survey of the ophthalmic use of anti-vascular endothelial growth factor drugs in Israel.

Waisbourd M, Goldstein M, Loewenstein A.

Department of Ophthalmology, Tel Aviv Sourasky Medical Center, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel. mwaisbourd@hotmail.com

BACKGROUND: Intravitreal injections of the anti-vascular endothelial growth factor (VEGF) drugs bevacizumab (Avastin) and ranibizumab (Lucentis) became the mainstay of treatment for various retinal pathologies, but there is no consensus among ophthalmologists on the precise use of these drugs.

OBJECTIVES: To describe the routine practices of retinal specialists in Israel regarding anti-VEGF drug treatment.

METHODS: A questionnaire was sent via email to all 62 members of the Israeli Society of Retinal Specialists. The survey included 34 questions on various aspects of the use of anti-VEGF drugs: diagnosis, treatment, follow-up of different retinal pathologies, and the measures taken for ensuring sterile administration of the intravitreal injections.

RESULTS: Fifty members (80%) completed the survey. Most of them (56%) offered both bevacizumab and ranibizumab to their patients for age-related macular degeneration, but 70% were influenced by the patient's socioeconomic status. Three consecutive monthly injections were usually recommended (58%) for the first 3 months, and treatment was extended as long as subretinal or intraretinal fluids persisted (57%). Over two-thirds (68%) switched the drugs after the 3-monthly series if the first one yielded no improvement in fluid status. The routine practice for intravitreal injection (> 80%) involved the wearing of sterile gloves, using an eyelid speculum, and administering povidone-iodine pretreatment and topical antibiotics after treatment.

CONCLUSIONS: Intravitreal VEGF administration varies widely among Israeli retinal specialists. The current survey is intended to assist Israeli ophthalmologists in establishing their own treatment strategy for patients with retinal pathologies.

PMID: 21608333 [PubMed - in process]

Other treatment & diagnosis

Semin Ophthalmol. 2011 May;26(3):65-8.

Vision rehabilitation of persons with age related macular degeneration.

Siemsen DW, Brown WL.

Department of Ophthalmology, Mayo Clinic, Rochester, Minnesota, USA.

Abstract

As the population of the United States ages, there is an increase in the number of persons with age related macular degeneration (ARMD). Even as new prevention and treatment techniques are developed, the vision loss associated with ARMD may lead to loss of independence and quality of life. Low vision is a rehabilitative process designed to improve visual function and restore independence. This paper is a review of the current research related to low vision in the areas of magnification, contrast and illumination, reading, training, driving and outcomes assessment.

PMID: 21609218 [PubMed - in process]

Semin Ophthalmol. 2011 May;26(3):94-103.

Retinal pigment epithelial tears and the management of exudative age-related macular degeneration.

Barkmeier AJ, Carvounis PE.

Department of Ophthalmology, Mayo Clinic, Rochester, MN.

Abstract

Tears of the retinal pigment epithelium (RPE) are a known and potentially catastrophic complication of exudative age-related macular degeneration (AMD). Eyes with vascularized retinal pigment epithelial detachments (PED) are especially at risk for the development of RPE tears. This long-recognized complication faces increased scrutiny in an era of improved anti-angiogenic treatments for AMD, particularly given that these newly developed therapeutics have been implicated as a potential factor in the formation of some RPE tears.

PMID: 21609221 [PubMed - in process]

Semin Ophthalmol. 2011 May;26(3):137-8.

Vitreomacular traction and age-related macular degeneration.

Green-Simms AE, Bakri SJ.

Department of Ophthalmology, Mayo Clinic, Rochester, MN, USA.

Abstract

The interaction between the vitreous and the internal limiting membrane of the retina is important in the pathoetiology of numerous ocular disease processes. Recent studies have focused on the vitreo-retinal interface in the context of age-related macular degeneration (AMD), linking vitreo-retinal adhesion to exudative AMD in particular. This review summarizes our knowledge of vitreous anatomy and recent investigations regarding vitreomacular adhesion and AMD.

PMID: 21609226 [PubMed - in process]

Semin Ophthalmol. 2011 May;26(3):225-33.

Imaging in neovascular age-related macular degeneration.

Gess AJ, Fung AE, Rodriguez JG.

California Pacific Medical Center, San Francisco, CA, USA.

Abstract

Imaging plays an essential role in the diagnosis and treatment of age-related macular degeneration (AMD). This review describes the imaging modalities most commonly employed by ophthalmologists caring for patients with neovascular AMD. Imaging modalities discussed include fluorescein angiography, optical coherence tomography, indocyanine green angiography, and fundus autofluorescence.

PMID: 21609236 [PubMed - in process]

Handb Clin Neurol. 2011;102:97-116.

Retinal disorders.

Landau K, Kurz-Levin M.

Abstract

The retina represents part of the central nervous system (CNS). After modifying the neural signal, the axon of the last neuron enters the optic nerve and leaves the eye. In most cases of retinal disease leading to visual loss, the diagnosis will be made by an ophthalmologist after examining the ocular fundus. Some retinal disorders, however, might not be detectable at the time of examination. Those patients will be referred to a neurologist for "unexplained visual loss" when suspecting a lesion behind the optic nerve. Moreover, knowledge of potential retinal abnormalities is useful for the neurologist when seeing patients with CNS disease, which can manifest itself also in the retina. This chapter aims to give an overview about retinal disorders causing no or only few retinal abnormalities, those associated with neurological diseases, as well as the most important retinal diseases involving the tissues of the ocular fundus (vitreous body, retina, pigment epithelium, and the choroid). The most frequently used examination techniques and diagnostic tools are described. Tumors, vascular disease, especially diabetic retinopathy, age-related macular degeneration, chorioretinal inflammatory and toxic disorders, paraneoplastic retinopathies, inherited retinal dystrophies, and retinal involvement in CNS disease such as phakomatoses and multiple sclerosis are discussed.

PMID: 21601064 [PubMed - in process]

Johns Hopkins Med Lett Health After 50. 2011 May;23(3):8.

Why can't I see at night and in low light as well as I used to?

[No authors listed]

PMID: 21528517 [PubMed - indexed for MEDLINE]

Semin Ophthalmol. 2011 May;26(3):216-24.

Induced pluripotent stem cell therapies for geographic atrophy of age-related macular degeneration.

Du H, Lim SL, Grob S, Zhang K.

Institute for Genomic Medicine and Shiley Eye Center, University of California at San Diego, La Jolla, CA, USA.

Abstract

There is currently no FDA-approved therapy for treating patients with geographic atrophy (GA), a late stage of age-related macular degeneration (AMD). Cell transplantation has the potential to restore vision in these patients. This review discusses how recent advancement in induced pluripotent stem (iPS) cells provides a promising therapy for GA treatment. Recent advances in stem cell biology have demonstrated that it is possible to derive iPS cells from human somatic cells by introducing reprogramming factors. Human retinal pigment epithelium (RPE) cells and photoreceptors can be derived from iPS cells by defined factors. Studies show that transplanting these cells can stabilize or recover vision in animal models. However, cell derivation protocols and transplantation procedures still need to be optimized. Much validation has to be done before clinical-grade, patient-derived iPS can be applied for human therapy. For now, RPE cells and photoreceptors derived from patient-specific iPS cells can serve as a valuable tool in elucidating the mechanism of pathogenesis and drug discovery for GA.

PMID: 21609235 [PubMed - in process]

Retina. 2011 May 21. [Epub ahead of print]

FUNCTIONAL AND MORPHOLOGIC BENEFITS IN EARLY DETECTION OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION USING THE PREFERENTIAL HYPERACUITY PERIMETER.

Lai Y, Grattan J, Shi Y, Young G, Muldrew A, Chakravarthy U.

From *The Royal Victoria Hospital, The Belfast Health and Social Care Trust, Belfast, Northern Ireland; †Centre for Vascular and Vision Sciences, The Queen's University of Belfast, Belfast, Northern Ireland; and ‡Shanxi Eye Hospital, PR China.

PURPOSE: To estimate the usefulness of preferential hyperacuity perimetry (PHP) in detecting conversion of early to late age-related macular degeneration in the Carotenoids and co-antioxidants in patients with Age-Related Maculopathy, a multicenter randomized controlled clinical trial.

METHODS: This was a nested case control study within the Carotenoids and co-antioxidants in patients with Age-Related Maculopathy (CARMA) clinical trial and included all participants enrolled in a single center (n = 200). Data are from participants who progressed to neovascular age-related macular degeneration (nvAMD) during time on study, Group 1 (n = 10) before the use of PHP and Group 2 (n = 10) during use of PHP. We also randomly selected 21 other participants (Group 3) who did not progress to nvAMD during time on study as a control group. Change in best-corrected visual acuity and contrast sensitivity and size of neovascular lesion at detection of conversion to nvAMD in Groups 1 and 2.

RESULTS: At detection of nvAMD, mean best-corrected visual acuity in Group 1 was 57.5 letters versus 67.4 in Group 2. In Group 1, the change in best-corrected visual acuity from baseline to detection of nvAMD was twice that of Group 2 (21.6 ± 9.0 versus 11.9 ± 10.7) with a mean difference of 9.7 letters (95% confidence interval, 0.41 to 19.0, P = 0.04, independent-samples t-test). The size of the neovascular lesion at detection was 3.06 mm in Group 1 versus 0.89 mm in Group 2 (P = 0.02). Two thirds of the participants in Group 2 were asymptomatic at detection of nvAMD compared with one fifth in Group 1. Preferential hyperacuity perimetry distortion maps were abnormal in 9 of 10 eyes in Group 2, which were confirmed by optical coherence tomography. Of the 21 eyes in Group 3, PHP maps were normal in 18 and abnormal in 3.

CONCLUSION: Preferential hyperacuity perimetry detected abnormalities in central visual function with high reliability. Eyes with nvAMD lesions detected by PHP had smaller lesions and better function when compared with the group before the introduction of PHP. The false-negative rate was <10% on PHP. The PHP distortion map was helpful in alerting clinicians to the presence of subclinical nvAMD.

PMID: 21610564 [PubMed - as supplied by publisher]

Epidemiology & pathogenesis

Ophthalmic Epidemiol. 2011 Jun;18(3):129-36.

The Prevalence of Age-Related Macular Degeneration in Italy (PAMDI) Study: Report 1.

Piermarocchi S, Segato T, Scopa P, Masetto M, Ceca S, Cavarzeran F, Peto T.

University of Padua, Padua, Italy.

Purpose: The present study aimed to estimate prevalence and risk factors associated with age-related macular degeneration (ARMD) in an Italian population and to analyze differences between urban and rural communities.

Methods: We conducted a population-based cross-sectional study among elderly residents in Northeast Italy. Participants were divided into urban and rural groups based on whether they lived in the city of Padova or the villages of Teolo and Torreglia, respectively. Fundus photographs were graded according to the International Classification for Age-related Maculopathy.

Results: A total of 1162 randomly selected subjects aged 61 years or more were invited to participate in the study. We examined 885 subjects, and 845 were eligible for fundus photograph grading. ARMD was estimated to affect 62.7% of the whole population (drusen 63-124 μm = 48.3%; drusen ≥125 μm = 10.4%; advanced ARMD = 4.1%). Age was confirmed as a risk factor for drusen ≥125 μm and advanced ARMD (Odds Ratio [OR] = 1.47, 95% Confidence Interval [CI] 1.28-1.69 and OR = 1.62, 95% CI 1.28-2.05, respectively, for a 5-year increase in age). The rural group appeared to be at a higher risk of developing large drusen compared to the urban sample (OR = 1.61, 95% CI 1.01-2.63) when adjusting for age and gender.

Conclusions: The results confirmed that ARMD affects a high percentage of the elderly population in Italy. This study does not support the hypothesis that living in a rural environment or belonging to a population of the Mediterranean basin may be protective against the intermediate stages of the disease.

PMID: 21609241 [PubMed - in process]

Zhonghua Yan Ke Za Zhi. 2011 Mar;47(3):273-275.

[Effects of diabetes mellitus on the occurrence of age-related macular degeneration.]

[Article in Chinese]

Li X, Wang YS.

Institute of Ophthalmology of Chinese PLA, Department of Ophthalmology, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, China.

Abstract

Diabetes mellitus causing long term disturbed glucose metabolism could result in tissue injury and multiple complications. According to recent studies, diabetes mellitus might be regarded as one of the risk factors of age related macular degeneration (AMD). Diabetes mellitus affects the incidence and progression of AMD through altering hemodynamics, increasing oxidative stress, accumulating advanced glycation end products, etc. By studying epidemiological investigation and basic research on this subject comprehensively, it is required to review the correlation between diabetes mellitus and AMD.

PMID: 21609629 [PubMed - as supplied by publisher]

Zhonghua Yan Ke Za Zhi. 2011 Apr;47(4):373-377.

[Alternative splicing of vascular endothelial growth factor A and ocular neovascularization.]

[Article in Chinese]

Fan SJ, He SZ.

Department of Ophthalmology, Chinese PLA General Hospital, Beijing 100853, China.

Abstract: Ocular neovascularization is the primary cause of blindness in a wide range of ocular diseases. The vascular endothelial growth factor A (VEGF-A) is the key factor involved in ocular angiogenesis, which can cause eye diseases through the development of pathological angiogenesis and increase of vascular permeability. There are two families of VEGF-A isoforms formed by alternative splicing, the angiogenic VEGF-A family (VEGF(xxx)), known to contribute to ocular neovascularization, and the anti-angiogenic VEGF-A family (VEGF(xxx)b), which is found in normal ocular tissues but downregulated in human diabetic retinopathy. The first member of the VEGF(xxx)b family to be isolated was VEGF(165)b. It can significantly reduce preretinal neovascularization without inhibition of physiological intraretinal angiogenesis. As the studies on the VEGF(xxx)b family proceed more deeply, controlling the balance of VEGF(xxx) to VEGF (xxx)b isoforms may be therapeutically valuable in the treatment of angiogenic eye diseases such as diabetic retinopathy and age-related macular degeneration.

PMID: 21612688 [PubMed - as supplied by publisher]

Eye Contact Lens. 2011 May 23. [Epub ahead of print]

Ultraviolet Radiation as a Risk Factor for Cataract and Macular Degeneration.

Roberts JE.

From the Department of Natural Sciences, Fordham University, NY.

ABSTRACT: The human eye is constantly exposed to sunlight and artificial lighting. Light transmission through the eye is fundamental to its unique biological functions of directing vision and circadian rhythm, and therefore, light absorbed by the eye must be benign. However, exposure to the intense ambient radiation can pose a hazard particularly if the recipient is over 40 years of age. This radiation exposure can lead to impaired vision and transient or permanent blindness.Both ultraviolet-A (UV-A) and UV-B induce cataract formation and are not necessary for sight. Ultraviolet radiation is also a risk factor for damage to the retinas of children. The removal of these wavelengths from ocular exposure will greatly reduce the risk of early cataract and retinal damage. One way this may be easily done is by wearing sunglasses that block wavelengths below 400 nm (marked 400 on the glasses). However, because of the geometry of the eye, these glasses must be wraparound sunglasses to prevent reflective UV radiation from reaching the eye. Additional protection may be offered by contact lenses that absorb significant amounts of UV radiation.In addition to UV radiation, short blue visible light (400-440 nm) is a risk factor for the adult human retina. This wavelength of light is not essential for sight and not necessary for a circadian rhythm response. For those over 50 years old, it would be of value to remove these wavelengths of light with specially designed sunglasses or contact lenses to reduce the risk of age-related macular degeneration.

PMID: 21617534 [PubMed - as supplied by publisher]

Mol Vis. 2011;17:1222-30. Epub 2011 May 6.

Transcriptional factors associated with epithelial-mesenchymal transition in choroidal neovascularization.

Hirasawa M, Noda K, Noda S, Suzuki M, Ozawa Y, Shinoda K, Inoue M, Ogawa Y, Tsubota K, Ishida S.

PURPOSE: To investigate the transcriptional factors associated with epithelial-mesenchymal transition (EMT) in choroidal neovascularization (CNV) secondary to age-related macular degeneration (AMD).

METHODS: Paraffin sections of CNV obtained from patients with AMD (n=12) were stained for transcriptional factors related to EMT, i.e., Snail, Slug, SIP1, and Twist. As a control, postmortem sections of ocular normal tissue were used. Furthermore, using a human retinal pigment epithelial (RPE) cell line (ARPE-19), reverse transcription-polymerase chain reaction (RT-PCR) and immunofluorescence microscopy were performed to explore the cellular localization and expression levels of EMT-associated transcriptional factors upon cytokine stimulation.

RESULTS: Of 12 specimens, 11 CNV tissues (91.6%) showed staining for Snail localized in cellular nuclei, particularly in those of RPE cells. Snail was strongly co-localized with α-smooth muscle antigen (SMA) in RPE cells. In contrast, postmortem human retina showed no Snail staining in RPE cells. Other transcriptional factors, Slug, Twist and SIP1 were not detected in CNV or normal human retina. In ARPE-19 cells, RT-PCR and immunofluorescence microscopy showed that Snail mRNA was upregulated by transforming growth factor (TGF)-β and VEGF stimulation. Furthermore, TGF-β induced relocalization of Snail to the nucleus in RPE cells.

CONCLUSIONS: The current data indicate that Snail is a major transcriptional factor for EMT changes of RPE cells in human CNV.

PMID: 21617757 [PubMed - in process]

J Mol Graph Model. 2011 May 6. [Epub ahead of print]

The effect of electrostatics on factor H function and related pathologies.

Kieslich CA, Vazquez H, Goodman GN, de Victoria AL, Morikis D.

Department of Bioengineering, University of California, Riverside, CA 92521, United States.

Abstract

Factor H (FH) contributes to the regulation of the complement system by binding to polyanionic surfaces and the proteins C3b/C3c/C3d. This implicates charge and electrostatic interactions in recognition and binding of FH. Despite the large amount of experimental and pathology data the exact mechanism at molecular level is not yet known. We have implemented a computational framework for comparative analysis of the charge and electrostatic diversity of FH modules and C3b domains to identify electrostatic hotspots and predict potential binding sites. Our electrostatic potential clustering analysis shows that charge distributions and electrostatic potential distributions are more useful in understanding C3b-FH interactions than net charges alone. We present a model of non-specific electrostatic interactions of FH with polyanion-rich surfaces and specific interactions with C3b, using our computational data and existing experimental data. We discuss the electrostatic contributions to the formation of the C3b-FH complex and the competition between FH and Factor Bb (Bb) for binding to C3b. We also discuss the significance of mutations of charged amino acids in the pathobiology of FH-mediated disease, such as age-related macular degeneration, atypical hemolytic uremic syndrome, and dense deposit disease. Our data can be used to guide future experimental studies.

PMID: 21605993 [PubMed - as supplied by publisher]

J Mol Neurosci. 2011 May 21. [Epub ahead of print]

ZIP2 and ZIP4 Mediate Age-Related Zinc Fluxes Across the Retinal Pigment Epithelium.

Leung KW, Gvritishvili A, Liu Y, Tombran-Tink J.

Department of Neural and Behavioral Sciences, College of Medicine, Pennsylvania State University, Hershey, PA, USA.

Abstract

Decreases in systemic and cellular levels of zinc (Zn(2+)) during normal aging correlate with several age-related pathologies including age-related macular degeneration. Zn(2+) homeostasis in tissues is not only dependent on dietary intake but also on optimal expression and function of its influx (ZIP) and efflux (ZnT) transporters. We recently showed that many of the Zn(2+) transporters are expressed by the retinal pigment epithelial (RPE) cells. In this study, we present evidence that RPE cells contain less endogenous Zn (2+) with increased aging and transport this ion vectorially with greater transport from the basal to apical direction. Expression of two Zn(2+) influx transporters, ZIP2 and ZIP4, is reduced as a function of RPE age. Gene silencing of ZIP2 and ZIP4 in RPE cells from young donors or their overexpression in cells from older donors confirms that these two transporters are essential in controlling Zn(2+) influx and sequestration in RPE cells. Both transporters are distributed on the basal surface of the RPE where they are likely to control Zn(2+) homeostasis in the outer retina.

PMID: 21603979 [PubMed - as supplied by publisher]

Genetics

Semin Ophthalmol. 2011 May;26(3):77-93.

Genetics of age-related macular degeneration: current concepts, future directions.

Deangelis MM, Silveira AC, Carr EA, Kim IK.

Ocular Molecular Genetics Institute, Massachusetts Eye and Ear Infirmary, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA.

Abstract

Age-related macular degeneration (AMD) is a progressive degenerative disease which leads to blindness, affecting the quality of life of millions of Americans. More than 1.75 million individuals in the United States are affected by the advanced form of AMD. The etiological pathway of AMD is not yet fully understood, but there is a clear genetic influence on disease risk. To date, the 1q32 (CFH) and 10q26 (PLEKHA1/ARMS2/HTRA1) loci are the most strongly associated with disease; however, the variation in these genomic regions alone is unable to predict disease development with high accuracy. Therefore, current genetic studies are aimed at identifying new genes associated with AMD and their modifiers, with the goal of discovering diagnostic or prognostic biomarkers. Moreover, these studies provide the foundation for further investigation into the pathophysiology of AMD by utilizing a systems-biology-based approach to elucidate underlying mechanistic pathways.

PMID: 21609220 [PubMed - in process]

Ophthalmic Epidemiol. 2011 Jun;18(3):137-42.

Age-related macular degeneration-susceptibility single nucleotide polymorphisms in a han chinese control population.

Hu J, Yuan Y, Shen L, Zhang J, Hu N, Guan H.

Department of Ophthalmology, Affiliated Hospital of Nantong University, Nantong, Jiangsu Province, China.

Purpose: Our study aimed to detect the frequency of age-related macular degeneration (AMD)-susceptibility single nucleotide polymorphisms (SNPs) in control subjects of Han Chinese in a population-based study.

Methods: A total of 419 subjects of Han Chinese without AMD were recruited from our population-based Nantong Eye Study. Nine AMD-susceptibility SNPs were genotyped. The allele/genotype frequencies were compared with the data from the literature and NCBI Reference Assembly.

Results: The call rates of genotyping were > 98%. All tested SNPs except for HTRA1 rs11200638 were in Hardy-Weinberg Equilibrium (HWE). The allele distributions of some AMD-susceptibility SNPs were different from the records for the Chinese population in the National Center for Biotechnology Information (NCBI) Reference Assembly. Compared to those in a Caucasian population, the frequency of minor alleles of CFH rs800292 (48% vs. 19.2%) and HTRA1 rs11200638 were much higher (47% vs. 25%), while the frequency of minor alleles of CFH rs1061170 (9% vs. 35%), CX3CR1 rs3732379 (3% vs. 21%), CX3CR1 rs3732378 (3% vs. 11%) and SERPING1 rs2511989 (11% vs. 48%) were much lower in the Han Chinese population. Minor differences were observed in the frequency of minor alleles of CFB rs4151667, C2 rs547154 and TLR3 rs3775291. The allele/genotype frequencies of CFH rs1061170 and HTRA1 rs11200638, two well-confirmed AMD-susceptible SNPs, were close to each other in the Han Chinese and Japanese population.

Conclusion: The distribution of AMD-susceptibility SNPs shows ethnicity specificity. Substantial differences of the SNPs' distribution were noted from study to study, even within the same ethnic group. The genotype data will be used for longitudinal observation of AMD onset in the follow-up of the cohort.

PMID: 21609242 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2011 May 25. [Epub ahead of print]

Evaluation of serum lipid concentrations and genetic variants at high-density lipoprotein metabolism loci and TIMP3 in age-related macular degeneration.

Fauser S, Smailhodzic D, Caramoy A, van de Ven JP, Kirchhof B, Hoyng CB, Klevering BJ, Liakopoulos S, den Hollander AI.

Department of Vitreoretinal Surgery, Center for Ophthalmology, University of Cologne, Germany;

Purpose: To analyse the association between polymorphisms in the TIMP3 gene and genes of the high-density lipoprotein (HDL) metabolism and age-related macular degeneration (AMD). To evaluate serum lipid and lipoprotein levels in AMD patients compared to control individuals.

Methods: Single nucleotide polymorphisms in or near the TIMP3, ABCA1, FADS1_3, CETP, LIPC and LPL genes were genotyped. Serum levels of apolipoprotein B (ApoB), apolipoprotein A2, lipoprotein a, cholesterol, triglycerides, and HDL-cholesterol were determined.

Results: Significant associations were found between AMD and variants in ABCA1 and FADS1_3, and a nearly significant association in TIMP3. No significant associations were observed for variants in LPL, LIPC and CETP. We also observed a significant elevation of ApoB levels in serum of AMD patients. Other lipids and lipoproteins were not significantly altered.

Conclusions: These results confirm associations of AMD with variants near theTIMP3 gene and at loci involved in HDL metabolism. They further highlight a role of the extracellular matrix and the HDL metabolism in the pathogenesis of AMD. This study identified increased ApoB levels as a possible new serum biomarker for AMD.

PMID: 21613373 [PubMed - as supplied by publisher]

Diet

Semin Ophthalmol. 2011 May;26(3):131-6.

Nutritional supplementation and age-related macular degeneration.

Olson JH, Erie JC, Bakri SJ.

Department of Ophthalmology, Mayo Clinic, Rochester, Minnesota, USA.

Abstract

The prevalence of Age-related macular degeneration (AMD) is increasing as the population of elderly in the United States grows. Currently the pathogenesis is not fully understood, however oxidative injury is felt to play a significant role. The Age-Related Eye Disease Study (AREDS) established that a supplemental combination of dietary antioxidants of zinc, β-carotene, vitamin C and vitamin E slowed progression of AMD. Recently lutein, zeaxanthin, B vitamins, and omega-3 fatty acids have also been reported to decrease AMD progression, while vitamin E and β-carotene where found to increase the risk of late AMD. AREDS2 is currently underway, further examining the effects of omega-3 fatty acids, carotenoids, and the original AREDS formulation. While awaiting the results of AREDS2, it is important to understand the evidence currently available, so that physicians can safely advise patients today. This review examines the most current literature available exploring nutritional supplementation in age-related macular degeneration.

PMID: 21609225 [PubMed - in process