Macular Disease Foundation AUSTRALIA
Our focus is your vision

MD Research News

Issue 117

Wednesday 13 February, 2012

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

Br J Ophthalmol. 2013 Feb 5. [Epub ahead of print]

Plasma levels of vascular endothelial growth factor before and after intravitreal injection of bevacizumab, ranibizumab and pegaptanib in patients with age-related macular degeneration, and in patients with diabetic macular oedema.

Zehetner C, Kirchmair R, Huber S, Kralinger MT, Kieselbach GF.

Medical University Innsbruck, Innsbruck, Austria.

AIMS: To determine the level of vascular endothelial growth factor (VEGF) in the plasma of patients with diabetic macular edema (DME) and of patients with exudative age-related macular degeneration (ARMD) before and after intravitreal injection of bevacizumab, ranibizumab or pegaptanib.

METHODS: 30 patients with DME and 30 patients with ARMD were included in this randomized controlled study. Patients were randomized to treatment with ranibizumab (0.5 mg), bevacizumab (1.25 mg) or pegaptanib (0.3 mg). 10 patients with DME received bevacizumab, 10 ranibizumab and 10 pegaptanib. The same randomized treatment allocation applied to the 30 patients with ARMD. The concentrations of VEGF were measured by ELISA just before the injection, after 7 days and 1 month.

RESULTS: Plasma VEGF in patients with exudative ARMD before the injection of bevacizumab was 89.7 pg/ml. It was significantly reduced to 25.1 pg/ml after 7 days (p=0.01), and to 22.8 pg/ml after 1 month (p=0.008). In patients with DME the same systemic reduction by bevacizumab was observed with a significant decrease of baseline VEGF level from 72.2 pg/ml to 13.7 pg/ml after 7 days (p=0.008) and 17.1 pg/ml at 4 weeks with (p=0.012). No significant reductions of plasma VEGF levels were observed in patients receiving ranibizumab or pegaptanib during follow-up.

CONCLUSIONS: Bevacizumab significantly reduces the level of VEGF in the blood plasma for up to one month in patients with DME as well as in those with ARMD. No significant systemic effects of intravitreal ranibizumab or pegaptanib on plasma VEGF could be observed.

PMID: 23385630 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2013 Feb 5. [Epub ahead of print]

Posterior vitreous detachment following intravitreal drug injection.

Geck U, Pustolla N, Baraki H, Atili A, Feltgen N, Hoerauf H.

Augenklinik der Universitätsmedizin Göttingen, Robert-Koch-Str. 40, 37075, Göttingen, Germany, ugeck@web.de.

BACKGROUND: To evaluate the incidence of posterior vitreous detachment (PVD) induced by intravitreal injection of different intravitreal drugs.

METHODS: This prospective observational study included 61 patients (61 eyes) with different underlying retinal diseases: exudative age-related macular degeneration (n = 47), cystoid macular edema (CME) after retinal vein occlusion (n = 8), and CME of other origin (n = 6). Bevazicumab (1.25 mg) was injected into 25 eyes, ranibizumab (0.5 mg) into 27 eyes, triamcinolone (4 mg) into six eyes, and a combination of bevacizumab and triamcinolone into three eyes. Patients with initial PVD were excluded. Patients were followed for at least 4-6 weeks after their last injection by Fourier-domain OCT, fundus biomicroscopy and ultrasound B-examination.

RESULTS: Overall, 15 of 61 eyes developed a PVD after intravitreal injection (n = 6 after ranibizumab, n = 7 after bevacizumab and n = 2 after triamcinolon) within a mean follow-up period of 11.1 weeks. PVD occurred in three eyes after the first injection, in three eyes after the second, and in seven eyes after the third injection. Incidence of PVD correlated with increasing age.

CONCLUSION: Intravitreal injection of commonly-used drugs seems to induce posterior vitreous detachment, which may thus influence the outcome of the underlying disease.

PMID: 23381655 [PubMed - as supplied by publisher]

Nihon Ganka Gakkai Zasshi. 2012 Dec;116(12):1150-5.

[Treatment guidelines for age-related macular degeneration]. [Article in Japanese]

Takahashi K, Ogura Y, Ishibashi T, Shiraga F, Yuzawa M.

Department of Ophthalmology, Kansai Medical University, 2-3-1 Shin-machi, Hirakata-shi, Osaka-fu 573-1191, Japan. takahask@hirakata.kmu.ac.jp

Abstract: We describe treatment guidelines for age-related macular degeneration (AMD) in Japan in line with the accepted classification and diagnostic criteria of AMD in Japan. A working group of five members drew up an AMD treatment algorithm based on a comprehensive review of foreign guidelines and recent data gathered in Japan. We applied lifestyle and dietary modifications and anti-oxidative supplementation to the prodromal stage of AMD and atrophic AMD. We recommend that, depending on the type of disease (typical AMD, polypoidal choroidal vasculopathy, or retinal angiomatous proliferation), an anti-vascular endothelial growth factor drug,

PMID: 23379205 [PubMed - in process]

Clin Ophthalmol. 2013;7:185-91. doi: 10.2147/OPTH.S40537. Epub 2013 Jan 24.

The effect of intravitreal bevacizumab and ranibizumab on cutaneous tensile strength during wound healing.

Christoforidis JB, Wang J, Jiang A, Willard J, Pratt C, Abdel-Rasoul M, Roy S, Powell H.

Department of Ophthalmology and Vision Science, College of Medicine, The University of Arizona, Tucson, AZ, USA.

PURPOSE: To investigate the effect of intravitreal bevacizumab and ranibizumab on wound tension and by

histopathology during cutaneous wound healing in a rabbit model and to compare this effect to placebo intravitreal saline controls 1 and 2 weeks following intravitreal injection.

METHODS: A total of 120 New Zealand white rabbits were randomly assigned to one of three treatment groups each consisting of 40 rabbits. Each group received intravitreal injections of bevacizumab, ranibizumab, or normal saline. Immediately afterwards, each rabbit underwent four 6 mm full-thickness dermatologic punch biopsies. Twenty rabbits from each agent group underwent wound harvesting on day 7 or day 14. The skin samples were stained for CD34 for vascular endothelial cells on day 7, and maximal wound tensile load was measured on days 7 and 14. Quantitative assessment of mean neovascularization (MNV) scores was obtained from 10 contiguous biopsy margin 400× fields of CD34-stained sections by two independent observers.

RESULTS: Wound tension reading means (N) with standard error and adjusted P-values on day 7 were: saline placebos, 7.46 ± 0.87; bevacizumab, 4.50 ± 0.88 (P = 0.041); and ranibizumab, 4.67 ± 0.84 (P = 0.025). On day 14 these were: saline placebos, 7.34 ± 0.55; bevacizumab, 6.05 ± 0.54 (P = 0.18); and ranibizumab 7.99 ± 0.54 (P = 0.40). MNV scores in CD34 stained sections were: saline controls, 18.31 ± 0.43; bevacizumab, 11.02 ± 0.45 (P < 0.0001); and ranibizumab, 13.55 ± 0.43 (P < 0.0001). The interobserver correlation coefficient was 0.928.

CONCLUSION: At day 7, both anti-vascular endothelial growth factor (anti-VEGF) agents had significantly suppressed MNV scores and exerted a significant reduction of cutaneous wound tensile strength compared with saline controls. At day 14, neither agent produced a significant effect on tensile wound strength. Since angiogenesis is an integral component of the proliferative phase of wound healing, we encourage clinicians to be aware of their patients' recent surgical history during intravitreal anti-VEGF therapy and to consider refraining from their use during the perioperative period.

PMID: 23378736 [PubMed] PMCID: PMC3559083

Graefes Arch Clin Exp Ophthalmol. 2013 Feb 7. [Epub ahead of print]

Minimizing the endophthalmitis rate following intravitreal injections using 0.25 % povidone-iodine irrigation and surgical mask.

Shimada H, Hattori T, Mori R, Nakashizuka H, Fujita K, Yuzawa M.

Department of Ophthalmology, School of Medicine, Surugadai Hospital of Nihon University, 1-8-13 Surugadai, Kanda, Chiyodaku, Tokyo, 101-8309, Japan, sshimada@olive.ocn.ne.jp.

BACKGROUND: To examine the efficacy of complying with an infection control manual for intravitreal injection of anti-vascular endothelial growth factor (VEGF) preparations in reducing the rate of endophthalmitis.

METHODS: We retrospectively reviewed intravitreal anti-VEGF injections conducted by vitreoretinal specialists at the outpatient injection room of a single university hospital between July 2009 and July 2012. The injections were conducted following an infection control manual established by our department. Doctors and nurses wore surgical masks, and disinfected the patient's eyelid skin with 10 % povidone-iodine and then the conjunctiva with 0.25 % povidone-iodine. After putting a drape on the patient's face, a lid speculum was placed. The conjunctival surface was again washed with 5 ml of 0.25 % povidone-iodine. After waiting at least 30 seconds, intravitreal injection was performed through povidone-iodine. Following injection, the injection site was again washed with 5 ml of 0.25 % povidone-iodine. Patients were treated with topical levofloxacin 4 times a day for 3 days before and after the injection.

RESULTS: A total of 15,144 injections comprising 548 injections of pegaptanib sodium, 846 injections of bevacizumab, and 13,750 injections of ranibizumab were performed. During this period, no case of suspected or proven infectious endophthalmitis occurred. The endophthalmitis rate was 0 per 15,144 injections, (95 % confidence interval, 0.0-0.0 %).

CONCLUSION: The results suggest that endophthalmitis can be reduced to a minimum by preventing normal flora of the conjunctiva and bacteria in the oral cavity from entering the vitreous. For this purpose, an infection control manual that requires nurses and doctors to wear surgical mask and drape the patient's face, irrigate the conjunctiva with 0.25 % povidone-iodine and wait at least 30 seconds before performing intravitreal injection is useful.

PMID: 23389553 [PubMed - as supplied by publisher]

Diabetes Res Clin Pract. 2013 Feb 4. pii: S0168-8227(13)00007-7. doi: 10.1016/j.diabres.2013.01.006. [Epub ahead of print]

Improvement of diabetic retinopathy with intravitreal Ranibizumab.

Kernt M, Cserhati S, Seidensticker F, Liegl R, Kampik A, Neubauer A, Ulbig MW, Reznicek L.

Department of Ophthalmology, Ludwig-Maximilians-Universiy, Munich, Germany. Electronic address: marcus.kernt@med.uni-muenchen.de.

Abstract: This study indicates that in addition to the significant improvement in visual acuity and reduction of central retinal thickness in patients with center-involving diabetic macular edema, intravitreal anti-VEGF treatment with Ranibizumab may also lead to a significant stabilization or even improvement of diabetic retinopathy.

PMID: 23391744 [PubMed - as supplied by publisher]

Br Med Bull. 2013 Feb 7. [Epub ahead of print]

What is new in the management of wet age-related macular degeneration?

Sivaprasad S, Hykin P.

Moorfields Eye Hospital, 162, City Road, EC1V 2PD London, UK.

Introduction or background: The hallmark of wet age-related macular degeneration (AMD) is choroidal neovascularization (CNV). The key cytokine involved in the pathogenesis of CNV is vascular endothelial growth factor (VEGF). Since 2005, antiVEGF therapy has revolutionized the management of this condition.

Sources of data: A systematic computerized literature search was conducted on PubMed (http://www.ncbi.nlm.nih.gov/pubmed/).

Areas of agreement: AntiVEGF therapy has resulted in improvement in visual function and performance. Currently, practitioners are spoilt for choice of these agents.

Areas of controversy: Bevacizumab is unlicensed for intraocular use but has a better market share than ranibizumab in the treatment of wet AMD as it is approximately 40 times cheaper than ranibizumab, if aliquoted into smaller doses for intraocular use. This has stirred up questions on indemnity, safety, dosing, treatment regimen and quality control, despite the fact that well-designed clinical trials have shown that both drugs are equally effective. Another dilemma for the physicians is the choice of treatment regimens with antiVEGF agents that include fixed dosing, optical coherence tomography (OCT)-guided re-treatment, treat and extend or a combination of proactive and reactive dosing. Real-life outcomes of physician-dependent OCT-guided re-treatment with these agents are inferior to outcomes reported in clinical trials.

Growing points: A recently food and drug administration-approved antiVEGF agent, aflibercept, is rapidly becoming a popular choice as well-designed randomized clinical trials indicate that eight weekly fixed dosing of aflibercept is non-inferior to monthly ranibizumab.

Areas timely for developing research: Options for reducing the frequency of repeated intravitreal injections are being explored. Combination therapy with photodynamic therapy and epimacular brachytherapy seem scientifically plausible due to their synergistic effects. However, so far the results on these combinations have not shown any superior visual outcomes to antiVEGF monotherapy, and the practicalities of delivering these therapies are formidable. So, research into other novel therapeutic approaches such as pigment epithelium-derived factor and designed ankyrin repeat proteins are gaining momentum.

PMID: 23393060 [PubMed - as supplied by publisher]

Klin Oczna. 2012;114(3):187-93.

Evaluation of treatment efficacy of intravitreal ranibizumab injections in patients with wet type of AMD.

Lubiński W, Mozolewska-Piotrowska K, Krasodomska K, Penkala K, Kaźmierczak B, Karczewicz D.

Department of Ophthalmology, Pomeranian Medical University, Szczecin, Poland.

PURPOSE: To evaluate foveal function, retinal circulation and foveal thickness before and after intravitreal ranibizumab injections in eyes with wet type of age-related macular degeneration (AMD).

MATERIAL AND METHODS: The study group consisted of 21 eyes (20 patients) with choroidal neovascularisation (CNV) due to AMD. Inclusion criteria were based on fluorescein angiography (FA) and distance best corrected visual acuity (DBCVA)--log MAR scale. In each eye, 3 consecutive injections of ranibizumab every 4 weeks were administered and then individual course for re-injections according to DBCVA and optical coherence tomography (OCT) up to 12 months was applied. At baseline, 3, 6 and 12 months follow-up, the following tests were performed: DBCVA, multifocal electroretinogram (mfERG) and OCT. Additionally, FA was carried out before the treatment, 3 and 12 months from the baseline.

RESULTS: At baseline, FA revealed mainly minimally occult choroidal neovascularisation--57% (12/21) of eyes. At 3 months choroidal neovascularisation diameter was stable; no leakage from active choroidal neovascularisation was seen in 76% (16/21) of eyes. After 12 months follow-up, increase in choroidal neovascularisation diameter was seen in 43% (9/21) of eyes and no leakage in 57% (12/21) of cases. The mean DBCVA significantly improved only after 3 months ($p < 0.02$). Significant decrease of mean foveal thickness was observed in each follow-ups ($p < 0.01$). The mfERG data from the macular region remained stable or improved slightly in some cases.

CONCLUSIONS: In our series of patients with the wet type of AMD after intravitreal injections of ranibizumab in 12 months follow-up, the reduction of foveal thickness was noted while DBCVA and the bioelectrical function from the macular region measured by the mfERG remained stable.

PMID: 23373399 [PubMed - in process]

Other treatment & diagnosis

J Neurol. 2013 Feb 5. [Epub ahead of print]

Charles Bonnet syndrome: two case reports and review of the literature.

Lerario A, Ciammola A, Poletti B, Girotti F, Silani V.

Department of Neurology and Laboratory of Neuroscience, IRCCS Istituto Auxologico Italiano, 20149, Milan, Italy, alberto.lerario@gmail.com.

Abstract: Visual hallucinations (VHs) can be associated with a variety of clinical conditions, and are also

experienced by healthy people due to visual impairment. The condition is known as Charles Bonnet Syndrome (CBS). The circumstances favoring VHs support the hypothesis that sensory deprivation enhances the ongoing activity of the visual system after sensory loss. Clinician should be aware that a significant proportion of visually impaired patients experience complex VHs, which are sometimes distressing. Herein, we report two cases of CBS. Case 1 is a 60-year-old man with visual impairment due to orbit pseudotumor in autoimmune hypothyroidism. Case 2 is an 87-year-old woman with Parkinson's disease and a 15-year history of intermittent complex VHs due to age-related macular degeneration in both eyes. In both cases investigations for alternative pathological causes of VHs were negative and, therefore, the aetiology of hallucinations was attributed to CBS. The course and treatment of CBS patients vary according to the nature of the visual dysfunction. Drug treatments remain partially satisfactory, with individual cases successfully treated with atypical antipsychotics. Nonpharmacological interventions aimed to reduce the visual pathway deprivation. Reassurance of the benign nature of CBS is essential to support patients and reduce caregiver's burden.

PMID: 23381616 [PubMed - as supplied by publisher]

Ophthalmologe. 2013 Feb 6. [Epub ahead of print]

[The influence of visual rehabilitation on secondary depressive disorders due to age-related macular degeneration : A randomized controlled pilot study.] [Article in German]

Mielke A, Wirkus K, Niebler R, Eschweiler G, Nguyen NX, Trauzettel-Klosinski S.

Department für Augenheilkunde, Sehbehindertenambulanz, Universität Tübingen, Schleichstr. 12-16, 72076, Tübingen, Deutschland.

BACKGROUND: Age-related macular degeneration (AMD) often leads to visual impairment, loss of reading ability, reduced quality of life and secondary depression. The present study examined if visual rehabilitation has a preventive effect on secondary depression in these patients.

MATERIAL AND METHODS: In a controlled pilot study 20 patients were randomized into 2 groups whereby 9 underwent visual rehabilitation at first examination and 11 received magnifying visual aids only after 3 months. Psychosocial status was assessed by the geriatric depression scale (GDS) and the German version of the Centre for Epidemiologic Studies depression (CES-D) scale (main outcome parameter), cognitive status by the dementia detection test (DemTecT), minimental status (MMS) and quality of life by the National Eye Institute visual function questionnaire (NEI-VFQ 25). Ophthalmological examination included reading speed measurement by standardized texts (International Reading Speed Texts; IReST).

RESULTS: Parameters of the CES-D scale, DemTect and the subitem exercise of social roles of the NEI-VFQ 25 emerged in a divergent manner. Patients of the rehabilitation group became less depressive and improved in cognitive and social abilities and in the control group vice versa. The interactive effect of group and time was statistically significant for all three tests.

CONCLUSIONS: Visual rehabilitation has a positive impact on depression as well as cognitive status and quality of life in patients with AMD. The effects have to be confirmed in future studies with more patients and a longer observation period.

PMID: 23380979 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2013 Feb 8. [Epub ahead of print]

Multifocal pupillography identifies retinal dysfunction in early age-related macular degeneration.

Sabeti F, James AC, Essex RW, Maddess T.

ARC Centre of Excellence in Vision Science, John Curtin School of Medical Research, Australian National University, Building 131, Garran Road, Acton, Canberra, ACT, 0200, Australia, faran.sabeti@anu.edu.au.

BACKGROUND: Early age-related macular degeneration (AMD) is common among the elderly. While only a small number progress to sight-threatening stages of AMD, identifying prognostic functional markers remains paramount. Here, we objectively evaluate retinal function in patients with large drusen by multifocal pupillographic objective perimetry (mfPOP). Different temporal presentation rates and luminances were compared to optimize parameters for high signal to noise ratios (SNR) and diagnosticity for early AMD.

METHODS: Pupil responses were recorded from 19 early AMD patients (30 eyes) and 29 age-matched control subjects. We compared a luminance-balanced stimulus ensemble and two unbalanced stimulus variants, each consisting of 44 independent stimulus regions per eye extending from fixation to 15˚ eccentricity. Video cameras recorded pupil responses for each eye under infrared illumination. The amplitudes and delays of the peak responses were analysed by multivariate linear models. The diagnostic accuracy of the stimulus variants was compared using areas under the curve (AUC) of receiver operator characteristic (ROC) plots.

RESULTS: Early AMD eyes differed significantly from normal in their mean constriction amplitudes (-2.22 ± 0.15 dB, t = -14.8) and delays (17.92 ± 1.2 ms, t = 14.9). The brightest stimulus ensembles produced the highest median SNRs of 3.45 z-score units; however, the balanced method was found to be the most diagnostic. AUC values of 0.95 ± 0.03 (mean ± SE) for early AMD were obtained when the asymmetry of response amplitudes between eyes was considered.

CONCLUSIONS: The mfPOP responses of early AMD eyes showed significant abnormality in response amplitudes and peak time. The ROC AUCs of 95 % suggest that mfPOP is a sensitive tool for detecting early abnormalities in AMD and longitudinal studies measuring progression of retinal dysfunction are warranted.

PMID: 23392820 [PubMed - as supplied by publisher]

Pathogenesis

PLoS One. 2013;8(2):e55372. doi: 10.1371/journal.pone.0055372. Epub 2013 Feb 1.

Analysis of the Cytoprotective Role of α-Crystallins in Cell Survival and Implication of the αA-Crystallin C-Terminal Extension Domain in Preventing Bax-Induced Apoptosis.

Hamann S, Métrailler S, Schorderet DF, Cottet S.

IRO, Institute for Research in Ophthalmology, Sion, Switzerland ; School of Life Sciences, Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland.

Abstract: α-Crystallins, initially described as the major structural proteins of the lens, belong to the small heat shock protein family. Apart from their function as chaperones, α-crystallins are involved in the regulation of intracellular apoptotic signals. αA- and αB-crystallins have been shown to interfere with the mitochondrial apoptotic pathway triggering Bax pro-apoptotic activity and downstream activation of effector caspases. Differential regulation of α-crystallins has been observed in several eye diseases such as age-related macular degeneration and stress-induced and inherited retinal degenerations. Although the function of α-crystallins in healthy and diseased retina remains poorly understood, their altered expression in pathological conditions argue in favor of a role in cellular defensive response. In the Rpe65(-/-) mouse model of Leber's congenital amaurosis, we previously observed decreased expression of αA- and αB-crystallins during disease progression, which was correlated with Bax pro-death activity and photoreceptor apoptosis. In the present study, we demonstrated that α-crystallins interacted with pro-apoptotic Bax and displayed cytoprotective action against Bax-triggered apoptosis, as assessed by TUNEL and caspase assays. We further observed in staurosporine-treated photoreceptor-like 661W cells stably overexpressing αA- or αB-crystallin

that Bax-dependent apoptosis and caspase activation were inhibited. Finally, we reported that the C-terminal extension domain of αA-crystallin was sufficient to provide protection against Bax-triggered apoptosis. Altogether, these data suggest that α-crystallins interfere with Bax-induced apoptosis in several cell types, including the cone-derived 661W cells. They further suggest that αA-crystallin-derived peptides might be sufficient to promote cytoprotective action in response to apoptotic cell death.

PMID: 23383327 [PubMed - in process] PMCID: PMC3562314

JAMA Ophthalmol. 2013 Feb 7:1-7. doi: 10.1001/jamaophthalmol.2013.2303. [Epub ahead of print]

C-Reactive Protein and the Incidence of Macular Degeneration: Pooled Analysis of 5 Cohorts.

Mitta VP, Christen WG, Glynn RJ, Semba RD, Ridker PM, Rimm EB, Hankinson SE, Schaumberg DA.

IMPORTANCE: This study adds to the evidence that elevated levels of high-sensitivity C-reactive protein (hsCRP) predict future risk of age-related macular degeneration (AMD). This information might shed light on underlying pathological mechanisms involving inflammation and could be of clinical utility in the identification of persons at high risk of AMD who may benefit from increased adherence to lifestyle recommendations, eye examination schedules, and therapeutic protocols.

OBJECTIVE To investigate the relationship between hsCRP and future risk of AMD in US men and women.

DESIGN: Pooled analysis of prospective nested case-control data from the Women's Health Study and 4 other cohorts, the Physicians' Health Study, Women's Antioxidant and Folic Acid Cardiovascular Study, Nurses' Health Study, and Health Professionals Follow-up Study.

SETTING: A prospective nested case-control study within 5 large cohorts.

PARTICIPANTS: Patients were initially free of AMD. We prospectively identified 647 incident cases of AMD and selected age- and sex-matched controls for each AMD case (2 controls for each case with dry AMD or 3 controls for each case of neovascular AMD).

MAIN OUTCOME MEASURES: We measured hsCRP in baseline blood samples. We used conditional logistic regression models to examine the relationship between hsCRP and AMD and pooled findings using meta-analytic techniques.

RESULTS: After adjusting for cigarette smoking status, participants with high (>3 mg/L) compared with low (<1 mg/L) hsCRP levels had cohort-specific odds ratios (ORs) for incident AMD ranging from 0.94 (95% CI, 0.58-1.51) in the Physicians' Health Study to 2.59 (95% CI, 0.58-11.67) in the Women's Antioxidant and Folic Acid Cardiovascular Study. After testing for heterogeneity between studies (Q = 5.61; P = .23), we pooled findings across cohorts and observed a significantly increased risk of incident AMD for high vs low hsCRP levels (OR, 1.49; 95% CI, 1.06-2.08). Risk of neovascular AMD was also increased among those with high hsCRP levels (OR, 1.84; 95% CI, 1.14-2.98).

CONCLUSIONS AND RELEVANCE: Overall, these pooled findings from 5 prospective cohorts add further evidence that elevated levels of hsCRP predict greater future risk of AMD. This information might shed light on underlying mechanisms and could be of clinical utility in the identification of persons at high risk of AMD who may benefit from increased adherence to lifestyle recommendations, eye examination schedules, and therapeutic protocols.

PMID: 23392454 [PubMed - as supplied by publisher]

J Huazhong Univ Sci Technolog Med Sci. 2013 Feb;33(1):137-41. doi: 10.1007/s11596-013-1086-y. Epub 2013 Feb 8.

Involvement of acid-sensing ion channel 1a in functions of cultured human retinal pigment epithelial cells.

Tan J, Xu YP, Liu GP, Ye XH.

Department of Plastic Surgery, Shanghai Tenth People's Hospital, Tongji University, Shanghai, 200072, China, j-tan@163.com.

Abstract: In the retina, pH fluctuations may play an important role in adapting retinal responses to different light intensities and are involved in the fine tuning of visual perception. Acidosis occurs in the subretinal space (SRS) under pathological conditions such as age-related macular degeneration (AMD). Although it is well known that many transporters in the retinal pigment epithelium (RPE) cells can maintain pH homeostasis efficiently, other receptors in RPE may also be involved in sensing acidosis, such as acid-sensing ion channels (ASICs). In this study, we investigated whether ASIC1a was expressed in the RPE cells and whether it was involved in the function of these cells. Real-time RT-PCR and Western blotting were used to analyze the ASIC1a expression in ARPE-19 cells during oxidative stress induced by hydrogen peroxide (H(2)O(2)). Furthermore, inhibition or over-expression of ASIC1a in RPE cells was obtained using inhibitors (amiloride and PCTx1) or by the transfection of cDNA encoding hASIC1a. Cell viability was determined by using the MTT assay. The real-time RT-PCR and Western blotting results showed that both the mRNA and protein of ASIC1a were expressed in RPE cells. Inhibition of ASICs by amiloride in normal RPE cells resulted in cell death, indicating that ASICs play an important physiological role in RPE cells. Furthermore, over-expression of ASIC1a in RPE cells prolonged cell survival under oxidative stress induced by H(2)O(2). In conclusion, ASIC1a is functionally expressed in RPE cells and may play an important role in the physiological function of RPE cells by protecting them from oxidative stress.

PMID: 23392723 [PubMed - in process]

Int Ophthalmol. 2013 Feb 3. [Epub ahead of print]

Association of dehydroepiandrosterone sulfate, serum lipids, C-reactive protein and body mass index with age-related macular degeneration.

Ulaş F, Balbaba M, Ozmen S, Celebi S, Doğan U.

Department of Ophthalmology, Abant Izzet Baysal University of Medicine, 14280, Bolu, Turkey, fatihu44@yahoo.com.

Abstract: The present study was designed to evaluate the associations between exudative age-related macular degeneration (AMD) and the serum concentrations of C-reactive protein (CRP), dehydroepiandrosterone sulfate (DHEAS), and lipids as well as the relationship between exudative AMD and body mass index (BMI). This cross-sectional study included of 141 healthy control subjects (70 males and 71 females with a mean age of 71.01 ± 3.84 years) and 142 exudative AMD patients (70 males and 72 females with a mean age of 70.92 ± 3.60 years). BMI and the serum concentrations of CRP, DHEAS, and lipids were measured in both groups. The data were statistically analysed using the Mann-Whitney U test, Chi squared test, independent sample t test, Cramer's V, point biserial correlation and logistic regression analysis. BMI values and serum concentrations of CRP, total cholesterol, and low-density lipoprotein (LDL) cholesterol were significantly higher in exudative AMD patients compared with normal controls (p values were 0.001, <0.001, 0.005 and <0.001, respectively). The serum concentrations of DHEAS were not significantly different between the controls and the exudative AMD patients for the subgroups of either gender (p values in males and females were 0.785 and 0.159, respectively). A logistic regression analysis revealed that the BMI and serum concentration of CRP moderately contributed to the predictive ability of the model (odds ratios were 1.205 and 1.179, respectively). Elevated total cholesterol concentrations and LDL cholesterol

concentrations, BMI values and serum concentrations of CRP were associated with exudative AMD. However, no association between the serum DHEAS concentration and exudative AMD was established.

PMID: 23377999 [PubMed - as supplied by publisher]

Ophthalmic Genet. 2013 Feb 1. [Epub ahead of print]

Complement Factor B Polymorphism and the Phenotype of Early Age-related Macular Degeneration.

Mantel I, Ambresin A, Moetteli L, Droz I, Roduit R, Munier FL, Schorderet DF.

Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital , Switzerland , and.

Abstract Purpose: Age-related macular degeneration (AMD) has been associated with a number of polymorphisms in genes in the complement pathway. We examined the potential genotype-phenotype correlation of complement factor B (CFB) (R32Q) polymorphisms in Caucasian patients with AMD.

Methods: Data from a Central European cohort of 349 patients with early AMD in at least one eye were analyzed for potential associations of the CFB (R32Q/rs641153) polymorphism with phenotypic features of early AMD. Early AMD was classified according to the International Classification and Grading System into predominant drusen size, largest drusen, drusen covered surface, central or ring-like location, peripheral drusen, and pigmentary changes. The potential association with single nucleotide polymorphisms on CFB (R32Q/rs641153) was evaluated for all patients, corrected for age, sex, and the polymorphisms of CFH (Y402H) and ARMS2 (A69S).

Results: CFB (R32Q) polymorphisms showed a significant association with smaller drusen size (largest drusen ≤250 µm, p = 0.021, predominant drusen ≤125 µm, p = 0.016), with smaller surface covered by drusen (≤10%; p = 0.02), and with more frequent occurrence of peripheral drusen (p = 0.007). No association was found for pigmentary changes.

Conclusions: The CFB (R32Q) polymorphism was associated with AMD characterized by small drusen only, and appeared to be protective of large drusen (OR 0.48/0.45) and of larger drusen covered area (OR 0.34). Furthermore, peripheral drusen were more frequently found (OR 2.27). This result supports the role of complement components and their polymorphisms in drusen formation and may enable a better understanding of AMD pathogenesis.

PMID: 23373431 [PubMed - as supplied by publisher]

Diet

Invest Ophthalmol Vis Sci. 2013 Feb 5. pii: iovs.12-10715v1. doi: 10.1167/iovs.12-10715. [Epub ahead of print]

Lutein supplementation over a one year period in early AMD might have a mild beneficial effect on visual acuity; the CLEAR study.

Murray IJ, Makridaki M, van der Veen RL, Carden D, Parry NR, Berendschot TT.

Faculty of Life Sciences, University of Manchester, Carys Bannister Building, Dover St, Manchester, M13 9PL, United Kingdom.

PURPOSE: To investigate the effect of daily supplementation with lutein (L) capsules on macular pigment optical density (MPOD) and visual acuity in early AMD (Age Related Macular Degeneration).

METHODS: A 12 month randomised, double-blind, placebo-controlled, two-centre investigation of the ef-

fects of L supplementation in early AMD was conducted. 72 patients (mean age 70.5 ± 8.7) were randomly assigned to either L (lutein, n=36) or P (placebo, n=36) groups. MPOD and best corrected visual acuity (LogMAR) were measured. Blood serum samples were collected RESULTS: Mean MPOD increased for the L group from 0.38±0.19 to 0.53±0.22 optical density (OD) units. A mixed design ANOVA showed this was statistically significant ($p<0.001$). There was no change in MPOD for the P group. There was no significant change in VA in the L group (n=36). The P group (n=36) showed a significant deterioration from 0.05 ± 0.13 to 0.09 ± 0.13, ($p < 0.05$). To avoid ceiling effects, 2 sub-groups of patients with VA worse than 0.06 at baseline were re-analysed. In the L sub-group (n= 19) a mean improvement in VA from 0.23±0.12 at baseline to 0.16±0.10 at visit 4 was observed ($p< 0.05$). The improvement in VA in the L sub-group was significant compared to the deterioration in the P group ($p<0.05$).

CONCLUSION: Lutein supplementation increases MPOD levels in early-stage AMD patients. VA measurements suggest the progress of AMD might be slowed in some patients with augmented levels of MP.

PMID: 23385792 [PubMed - as supplied by publisher]