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Drug treatment

J Pharm Sci. 2012 Dec 4. doi: 10.1002/jps.23387. [Epub ahead of print]

Characterization of human sclera barrier properties for transscleral delivery of bevacizumab and ranibizumab.

Wen H, Hao J, Li SK.

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Abstract: The objectives of this study were to (a) investigate transscleral permeation of antivascular endothelial growth factor drugs bevacizumab and ranibizumab and (b) examine the effects of molecular structures of macromolecules upon permeation across human sclera using bevacizumab, ranibizumab, fluorescein isothiocyanate (FITC)-labeled bovine serum albumin (FITC-BSA), FITC-labeled ficoll (FITC-ficoll), and FITC-labeled dextrans (FITC-dextrans) in vitro. The hydrodynamic radii of the macromolecules were measured using dynamic light scattering, their partition coefficients to sclera were determined in uptake experiments, and their permeability coefficients and transport lag times across sclera were evaluated in transport experiments of side-by-side diffusion cells. Macromolecules showed relatively low partition coefficients to sclera. The partition coefficient of FITC-BSA was found to be related to its concentration in the equilibration solution, whereas for other macromolecules, no specific concentration dependency was observed. The macromolecules displayed relatively low permeability coefficients and long transport lag times because of their molecular sizes and hindered diffusion. Bevacizumab, ranibizumab, and FITC-BSA exhibited lower transscleral permeability and longer transport lag times than FITC-dextrans and FITC-ficoll of comparable molecular weights possibly because of the flexible structures of the polysaccharides. Thus, the polysaccharides may not be good surrogate permeants to model transscleral transport of therapeutic proteins in transscleral delivery studies. © 2012 Wiley Periodicals, Inc. and the American Pharmacists Association J Pharm Sci.

PMID: 23212655 [PubMed - as supplied by publisher]

Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2012 Nov 28. doi: 10.5507/bp.2012.100. [Epub ahead of print]

Effects of treatment change in patients with neovascular age-related macular degeneration; Results from the Czech National Registry.

Studnicka J, Rencova E, Rozsival P, Dusova J, Dubska Z, Chrapek O, Kolar P, Kandrnal V, Pitrova S,

Rehak J.

Department of Ophthalmology, Faculty of Medicine in Hradec Kralove, Charles University in Prague and University Hospital in Hradec Kralove, Czech Republic.

AIMS: To determine the effectiveness of second line treatments in patients with neovascular AMD who did not respond adequately to primary treatment.

METHODS: Retrospective, multicentre assessment. The frequency of primary treatment failure and outcomes of subsequent secondary treatment were assessed according to the type of primary treatment, type of CNV and change in BCVA over a 12 month period.

RESULTS: At the time of assessment 750 entries (750 treated eyes, 725 treated patients) had follow-up longer than 12 months. A treatment change required 7.7% subjects treated with ranibizumab, 20.5% with pegaptanib and 22% with PDT and verteporfin. Average BCVA of all patients at the beginning of primary treatment was 50.7 ± 3 letters and 43 ± 3.5 letters in 12(th) month (P<0.001). The mean decrease in BCVA was 7.7 ± 0.6 letters during the first 6 months of observation. During the next 6 months, no significant change occurred. The change of primary therapy was required on average after 6.5 ± 2.1 months.

CONCLUSION: BCVA loss was the most significantly decelerated in patients who received ranibizumab as a secondary therapy following unsuccessful treatment with pegaptanib sodium.

PMID: 23202275 [PubMed - as supplied by publisher]

Jpn J Ophthalmol. 2012 Dec 4. [Epub ahead of print]

Two-year results of combined intravitreal anti-VEGF agents and photodynamic therapy for retinal angiomatous proliferation.

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PURPOSE: To clarify the efficacy of a combination of intravitreal anti-vascular endothelial growth factor (VEGF) injections and photodynamic therapy (PDT), over 24 months, for patients with symptomatic retinal angiomatous proliferation (RAP).

METHODS: We retrospectively reviewed 13 treatment-naïve eyes of 12 patients (7 men, 5 women; age range (mean), 63-92 (77) years) treated with intravitreal bevacizumab (IVB) plus PDT as initial treatment. Retreatment was performed with IVB plus PDT until February 2009 or intravitreal ranibizumab and PDT from March 2009.

RESULTS: Mean best-corrected visual acuity (BCVA) significantly improved from 0.26 at baseline to 0.40 at 24 months (P = 0.013). The mean improvement in BCVA at 24 months from baseline was 1.79 lines. The central retinal thickness decreased significantly from 431 to 142 microns at 24 months (P < 0.0001). Complete occlusion of the retinal-retinal anastomosis was achieved in seven of the 10 eyes at 24 months. The mean number of PDT treatments during 24 months was 2.8 and the mean number of injections was 3.4. Geographic atrophy was seen in four eyes without significant decline of VA at 24 months.

CONCLUSION: Combined anti-VEGF and PDT for RAP patients effectively maintained or improved VA and reduced exudation, without severe adverse events, over 24 months.

PMID: 23208024 [PubMed - as supplied by publisher]

Expert Opin Pharmacother. 2012 Nov 30. [Epub ahead of print]

Current status of unoprostone for the management of glaucoma and the future of its use in the treatment of retinal disease.

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Introduction: Optic nerve and retinal diseases such as glaucoma, age-related macular degeneration (AMD) and retinitis pigmentosa (RP) are significant public health concerns and have a momentous impact on patients' functional status and quality of life. These diseases are among the most common causes of visual impairment worldwide and account for billions of dollars in healthcare expenditures and lost productivity. The importance of adequate treatment of these conditions and the need for efficacious therapeutic drugs cannot be overstated. Unoprostone continues to be developed as a potential treatment for these debilitating diseases.

Areas covered: This review provides background information on unoprostone isopropyl (unoprostone), a prostanoid and synthetic docosanoid approved for the treatment of open-angle glaucoma and ocular hypertension, and recapitulates safety and efficacy data as it relates to this indication. Additionally, this review describes potential new uses of unoprostone as therapy for dry AMD and RP. A literature search of peer-reviewed publications was performed utilizing PubMed. Searches were last updated on 10 September 2012.

Expert opinion: Current data indicate that unoprostone does significantly lower intraocular pressure (IOP) and has a favorable safety and tolerability profile. However, the IOP-lowering effects of unoprostone do not compare with other commercially available prostanoids and it has the disadvantage of a twice-daily rather than once-daily dosing regimen. Nonetheless, recent data suggest that unoprostone may improve neuronal survival and increase ocular blood flow, indicating that it may have some value as a therapy for glaucoma, RP and dry AMD. Further studies are needed to confirm whether unoprostone provides any clinically significant advantage over the other commercially available prostanoids.

PMID: 23199345 [PubMed - as supplied by publisher]

Other treatment & diagnosis

J Fr Ophtalmol. 2012 Nov 27. pii: S0181-5512(12)00333-6. doi: 10.1016/j.jfo.2012.09.002. [Epub ahead of print]

[Idiopathic macular telangiectasia: Clinical appearance, imaging and treatment.]

[Article in French]

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INTRODUCTION: This work aims to summarize the clinical features of idiopathic macular telangiectasia (IMT) and the role of imaging in this condition as well as to review available treatments.

PATIENTS AND METHODS: This is a retrospective analysis of IMT patients diagnosed, followed and treated between June 2010 and March 2012 at the Red Cross Hospital in Lyon. Patients were identified on the basis of Yanuzzi classification. Funduscopic appearance, fluorescein angiography, autofluorescence photos and high-resolution spectral domain ocular coherence tomography (SD-OCT) allowed these IMT

patients to be classified into two groups. Patients with visual loss secondary to cystoid macular edema were treated with laser and/or intravitreal anti-VEGF injection.

RESULTS: Four patients were examined on the basis of decreased visual acuity secondary to IMT. The combination of fluorescein angiography and SD-OCT allowed the diagnosis of two patients as group 1 IMT and two patients as group 2 IMT. Patients with group 1 telangiectasias were treated by laser and/or intravitreal anti-VEGF. We found functional and anatomical efficacy of anti-VEGF treatment for group 1 IMT.

DISCUSSION: The physiopathology of IMT is complex and still remains imperfectly understood. Anti-VEGF treatment appears to be an effective alternative for the treatment of cystoid macular edema in group 1 IMT.

CONCLUSION: The physiopathology of IMT is very complex. We have shown that anti-VEGF seems to give satisfactory results for cystoid macular edema in group 1 IMT, although several reinjections may be required. It seems that there is no effective treatment for group 2 IMT without neovascular complications. Future therapeutic progress in the treatment of atrophic age-related macular degeneration will probably be effective in this condition as well.

PMID: 23200165 [PubMed - as supplied by publisher]

J Vis Exp. 2012 Nov 25;(69). pii: 4286. doi: 10.3791/4286.

Subretinal injection of gene therapy vectors and stem cells in the perinatal mouse eye.

Wert KJ, Skeie JM, Davis RJ, Tsang SH, Mahajan VB.

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Abstract: The loss of sight affects approximately 3.4 million people in the United States and is expected to increase in the upcoming years.(1) Recently, gene therapy and stem cell transplantations have become key therapeutic tools for treating blindness resulting from retinal degenerative diseases. Several forms of autologous transplantation for age-related macular degeneration (AMD), such as iris pigment epithelial cell transplantation, have generated encouraging results, and human clinical trials have begun for other forms of gene and stem cell therapies.(2) These include RPE65 gene replacement therapy in patients with Leber's congenital amaurosis and an RPE cell transplantation using human embryonic stem (ES) cells in Stargardt's disease.(3-4) Now that there are gene therapy vectors and stem cells available for treating patients with retinal diseases, it is important to verify these potential therapies in animal models before applying them in human studies. The mouse has become an important scientific model for testing the therapeutic efficacy of gene therapy vectors and stem cell transplantation in the eye.(5-8) In this video article, we present a technique to inject gene therapy vectors or stem cells into the subretinal space of the mouse eye while minimizing damage to the surrounding tissue.

PMID: 23207897 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2012 Dec 3;53(13). pii: 7950. doi: 10.1167/iovs.12-11224.

Author Response: Validation of the National Eye Institute Visual Function Questionnaire-25 (NEIVFQ-25) in Age-Related Macular Degeneration.

Orr P, Rentz AM, Margolis MK, Revicki DA, Dolan CM, Colman S, Fine JT, Bressler NM.

Retina Division, Wilmer Eye Institute, Department of Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland.

PMID: 23208790 [PubMed - in process]

Pathogenesis

J Cell Mol Med. 2012 Dec 4. doi: 10.1111/j.1582-4934.2012.01652.x. [Epub ahead of print]

Characterization of stress response in human retinal epithelial cells.

Giansanti V, Villalpando Rodriguez GE, Savoldelli M, Gioia R, Forlino A, Mazzini G, Pennati M, Zaffaroni N, Scovassi AI, Torriglia A.

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Abstract: The pathogenesis of age-related macular degeneration (AMD) involves demise of the retinal pigment epithelium and death of photoreceptors. In this article, we investigated the response of human adult retinal pigmented epithelial (ARPE-19) cells to 5-(N,N-hexamethylene)amiloride (HMA), an inhibitor of Na(+) /H(+) exchangers. We observed that ARPE-19 cells treated with HMA are unable to activate 'classical' apoptosis but they succeed to activate autophagy. In the first 2 hrs of HMA exposure, autophagy is efficient in protecting cells from death. Thereafter, autophagy is impaired, as indicated by p62 accumulation, and this protective mechanism becomes the executioner of cell death. This switch in autophagy property as a function of time for a single stimulus is here shown for the first time. The activation of autophagy was observed, at a lesser extent, with etoposide, suggesting that this event might be a general response of ARPE cells to stress and the most important pathway involved in cell resistance to adverse conditions and toxic stimuli.

PMID: 23205553 [PubMed - as supplied by publisher]

Yakugaku Zasshi. 2012;132(12):1365-70.

Non-invasive ophthalmic liposomes for nucleic Acid delivery to posterior segment of eye.

Takashima Y, Tsuchiya T, Igarashi Y, Kanazawa T, Okada H, Urtti A.

Pharmaceutical Technology, School of Pharmacy, Tokyo University of Pharmacy and Life Sciences.

Abstract: Nucleic acids like siRNA and pDNA are remarkable for treatment of ophthalmic diseases in posterior segment of eye such as age-related macular degeneration (AMD). However, hydrophilic and high molecule compounds are restricted in intraocular distribution through anterior segment of the eye. In addition, the ocular tissue has a blood-retinal barrier which restricts drug delivery thorough systemic administration. Therefore the invasive intravitreal injection has been generally applied for treatment of retinal diseases. The objective in this study is to prepare nucleic acid-loaded liposomes for effective gene delivery to posterior segment of eye by non-invasive ophthalmic administration such as eye-drops. The pDNA/PEI-complex loaded liposomes were prepared using detergent removal method. The obtained liposomes were lyophilized with optimal amount of a cryoprotectant to avoid changes in physical properties and, followed by adjustment of an appropriate volume and osmotic pressure as ophthalmic solution. The liposomes show high pDNA encapsulation efficiency and good cellular uptake ability in human retinal pigment epithelial cells (ARPE-19 cells). We further demonstrate that the modification of ligand which binds to specific receptor on the RPE cells to the liposomes may improve gene delivery efficacy to the posterior segment of eye by non-invasive ocular instillation.

PMID: 23208042 [PubMed - in process]

Mediators Inflamm. 2012;2012:546786. doi: 10.1155/2012/546786. Epub 2012 Nov 7.

Mechanism of inflammation in age-related macular degeneration.

Parmeggiani F, Romano MR, Costagliola C, Semeraro F, Incorvaia C, D'Angelo S, Perri P, De Palma P, De

Nadai K, Sebastiani A.

Department of Ophthalmology, University of Ferrara, Ferrara, Italy.

Abstract: Age-related macular degeneration (AMD) is a multifactorial disease that represents the most common cause of irreversible visual impairment among people over the age of 50 in Europe, the United States, and Australia, accounting for up to 50% of all cases of central blindness. Risk factors of AMD are heterogeneous, mainly including increasing age and different genetic predispositions, together with several environmental/epigenetic factors, that is, cigarette smoking, dietary habits, and phototoxic exposure. In the aging retina, free radicals and oxidized lipoproteins are considered to be major causes of tissue stress resulting in local triggers for parainflammation, a chronic status which contributes to initiation and/or progression of many human neurodegenerative diseases such as AMD. Experimental and clinical evidences strongly indicate the pathogenetic role of immunologic processes in AMD occurrence, consisting of production of inflammatory related molecules, recruitment of macrophages, complement activation, microglial activation and accumulation within those structures that compose an essential area of the retina known as macula lutea. This paper reviews some attractive aspects of the literature about the mechanisms of inflammation in AMD, especially focusing on those findings or arguments more directly translatable to improve the clinical management of patients with AMD and to prevent the severe vision loss caused by this disease.

PMID: 23209345 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2012 Dec 4. pii: iovs.12-10281v1. doi: 10.1167/iovs.12-10281. [Epub ahead of print]

PATHOGENIC ROLE OF THE WNT SIGNALING PATHWAY ACTIVATION IN LASER-INDUCED CHOROIDAL NEOVASCULARIZATION.

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PURPOSE: Choroidal neovascularization (CNV) is a severe complication of age-related macular degeneration (AMD). The Wnt signaling pathway has been shown to mediate angiogenesis. The purpose of this study was to investigate the pathogenic role of the Wnt pathway in CNV and explore the therapeutic potential of a novel Wnt signaling inhibitor in CNV.

METHODS: Adult rats and mice were photocoagulated using diode laser to induce CNV. On the same day, the animals were intravitreally injected with a monoclonal antibody (Mab2F1) blocking LRP6 or non-specific mouse IgG. The Wnt signaling activation and target gene expression in the eyecup were determined by Western blot analysis. The fundus angiography was used to examine leakage from the laser lesion. CNV areas were measured on choroidal flatmount using FITC-dextran.

RESULTS: Levels of Wnt pathway components and Wnt target gene expression were elevated in both laser-induced CNV rat and mouse eyecups, suggesting activation of the Wnt pathway. Significant suppression of Wnt signaling was observed in the Mab2F1 treatment group. Mab2F1 decreased vascular leakage from CNV lesions and reduced the neovascular area in laser-induced CNV rats. Mab2F1 inhibited the hypoxia-induced activation of Wnt signaling in cultured RPE cells. Mab2F1 also ameliorated retinal inflammation and vascular leakage in the eyecups of very low-density lipoprotein receptor knockout mice, a model of sub-retinal neovascularization.

CONCLUSIONS: The Wnt pathway is activated in the laser-induced CNV models and plays a pathogenic role in CNV. Blockade of Wnt signaling using an anti-LRP6 antibody has therapeutic potential in CNV.

PMID: 23211829 [PubMed - as supplied by publisher]

Genetics

Korean J Ophthalmol. 2012 Dec;26(6):423-7. doi: 10.3341/kjo.2012.26.6.423. Epub 2012 Nov 12.

Association between Exudative Age-related Macular Degeneration and the G6721T Polymorphism of XRCC7 in Outdoor Subjects.

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PURPOSE: To investigate whether the G6721T polymorphism (rs.7003908) of the non-homologous end-joining DNA repair XRCC7 gene contributes to the development of exudative age-related macular degeneration (ARMD).

METHODS: The present case-control study consisted of 111 patients with exudative ARMD and 112 sex frequency-matched healthy controls that were randomly selected from unrelated volunteers in the same clinic. Genotypes were determined by the Restriction Fragment Length Polymorphism (PCR-RFLP) based method. Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for ARMD risk associated with polymorphism of XRCC7. In all analysis the GG genotype was considered to be the reference genotype.

RESULTS: There was no significant association between genotypes of XRCC7 and susceptibility to ARMD. Considering the significant difference in age distribution between cases and controls, age was used as a covariate in further analysis. After ORs were adjusted for age, the same result was observed. In the next step we stratified our subjects into outdoor and indoor groups according to their job titles. The outdoor and indoor patients were occupationally exposed to sunlight and not exposed to sunlight, respectively. Our present study showed that among indoor subjects there was no association between XRCC7 polymorphism and susceptibility to ARMD. However, among outdoor subjects, the GT + TT genotypes compared to the GG genotype increased the risk of ARMD (OR, 3.13; 95% CI, 1.04-9.39; p = 0.042).

CONCLUSIONS: Our study revealed that the T allele of the G6721T polymorphism of XRCC7 increased the risk of ARMD among outdoor subjects.

PMID: 23204796 [PubMed - in process]

Korean J Ophthalmol. 2012 Dec;26(6):414-22. doi: 10.3341/kjo.2012.26.6.414. Epub 2012 Nov 12.

Pharmacogenetic Influence of LOC387715/HTRA1 on the Efficacy of Bevacizumab Treatment for Age-Related Macular Degeneration in a Korean Population.

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PURPOSE: The purpose of this study was to determine the pharmacogenetic effects of complement factor H (CFH) Y402H, LOC387715 and high-temperature requirement factor A1 (HTRA1) genotypes on the treatment of exudative age-related macular degeneration (AMD) by intravitreal bevacizumab injection in a Korean population.

METHODS: Seventy-five patients diagnosed with exudative AMD were treated with intravitreal bevacizumab (2.5 mg) monotherapy. All patients received three initial intravitreal bevacizumab injections every four weeks and were then treated "as needed" based on clinical findings, optical coherence tomography and fluorescein angiography during the 12 month follow-up period after the third injection.

RESULTS: The difference in visual acuity improvement among the three genotypes of LOC387715 were statistically significant at six months post-treatment (logarithm of the minimum angle of resolution; TT, 0.346; GT, 0.264; GG, 0.188; p = 0.037). Among the LOC387715 genotypes, the number of additional injections was lower in patients who had the risk T allele (GG, 2.143; GT, 2.000; TT, 1.575; p = 0.064). There was no significant difference between visual acuity and central macular thickness change in the CFH Y402H polymorphism group during the 12 month follow-up period. However, the TC group of CFH Y402H required more additional bevacizumab injections than the TT group (TT, 1.517; TC, 3.363; p = 0.020).

CONCLUSIONS: This study demonstrated that different LOC387715/HTRA1 genotypes resulted in different bevacizumab treatment responses on exudative AMD. Patients with the risk allele had an improved treatment response and less need for additional injections. However, patients with the CFH Y402H risk allele needed more additional injections of bevacizumab in order to improve visual acuity. This study illustrates how pharmacogenetic factors may help determine treatment modality and dosing. This could ultimately provide basic data for 'personalized medicine' in AMD.

PMID: 23204795 [PubMed - in process]

Int J Mol Sci. 2012 Oct 18;13(10):13378-97. doi: 10.3390/ijms131013378.

Genetic variability in DNA repair proteins in age-related macular degeneration.

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Abstract: The pathogenesis of age-related macular degeneration (AMD) is complex and involves interactions between environmental and genetic factors, with oxidative stress playing an important role inducing damage in biomolecules, including DNA. Therefore, genetic variability in the components of DNA repair systems may influence the ability of the cell to cope with oxidative stress and in this way contribute to the pathogenesis of AMD. However, few reports have been published on this subject so far. We demonstrated that the c.977C>G polymorphism (rs1052133) in the hOGG1 gene and the c.972G>C polymorphism (rs3219489) in the MUTYH gene, the products of which play important roles in the repair of oxidatively damaged DNA, might be associated with the risk of AMD. Oxidative stress may promote misincorporation of uracil into DNA, where it is targeted by several DNA glycosylases. We observed that the g.4235T>C (rs2337395) and c.-32A>G (rs3087404) polymorphisms in two genes encoding such glycosylases, UNG and SMUG1, respectively, could be associated with the occurrence of AMD. Polymorphisms in some other DNA repair genes, including XPD (ERCC2), XRCC1 and ERCC6 (CSB) have also been reported to be associated with AMD. These data confirm the importance of the cellular reaction to DNA damage, and this may be influenced by variability in DNA repair genes, in AMD pathogenesis.

PMID: 23202958 [PubMed - in process]

PLoS One. 2012;7(11):e50181. doi: 10.1371/journal.pone.0050181. Epub 2012 Nov 29.

Effect of the Gas6 c.834+7G>A Polymorphism and the Interaction of Known Risk Factors on AMD Pathogenesis in Hungarian Patients.

Losonczy G, Vajas A, Takács L, Dzsudzsák E, Fekete A, Márhoffer E, Kardos L, Ajzner E, Hurtado B, de Frutos PG, Berta A, Balogh I.

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Abstract: Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly in the

developed world. Numerous genetic factors contribute to the development of the multifactorial disease. We performed a case-control study to assess the risk conferred by known and candidate genetic polymorphisms on the development of AMD. We searched for genetic interactions and for differences in dry and wet AMD etiology. We enrolled 213 patients with exudative, 67 patients with dry AMD and 106 age and ethnically matched controls. Altogether 12 polymorphisms in Apolipoprotein E, complement factor H, complement factor I, complement component 3, blood coagulation factor XIII, HTRA1, LOC387715, Gas6 and MerTK genes were tested. No association was found between either the exudative or the dry form and the polymorphisms in the Apolipoprotein E, complement factor I, FXIII and MerTK genes. Gas6 c.834+7G>A polymorphism was found to be significantly protective irrespective of other genotypes, reducing the odds of wet type AMD by a half (OR=0.50, 95%CI: 0.26-0.97, p=0.04). Multiple regression models revealed an interesting genetic interaction in the dry AMD subgroup. In the absence of C3 risk allele, mutant genotypes of both CFH and HTRA1 behaved as strongly significant risk factors (OR=7.96, 95%CI: 2.39=26.50, p=0.0007, and OR=36.02, 95%CI: 3.30-393.02, p=0.0033, respectively), but reduced to neutrality otherwise. The risk allele of C3 was observed to carry a significant risk in the simultaneous absence of homozygous CFH and HTRA1 polymorphisms only, in which case it was associated with a near -five-fold relative increase in the odds of dry type AMD (OR=4.93, 95%CI: 1.98-12.25, p=0.0006). Our results suggest a protective role of Gas6 c.834+7G>A polymorphism in exudative AMD development. In addition, novel genetic interactions were revealed between CFH, HTRA1 and C3 polymorphisms that might contribute to the pathogenesis of dry AMD.

PMID: 23209669 [PubMed - in process]

Diet

Br J Nutr. 2012 Dec 5:1-12. [Epub ahead of print]

Serum response to supplemental macular carotenoids in subjects with and without age-related macular degeneration.

Meagher KA, Thurnham DI, Beatty S, Howard AN, Connolly E, Cummins W, Nolan JM.

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Abstract: Macular pigment (MP) is composed of lutein (L), zeaxanthin (Z) and meso-zeaxanthin (MZ). The present study reports on serum response to three different MP supplements in normal subjects (n 27) and in subjects with age-related macular degeneration (AMD) (n 27). Subjects were randomly assigned to: Group 1 (20 mg L and 2 mg Z), Group 2 (10 mg L, 2 mg Z and 10 mg MZ) or Group 3 (3 mg L, 2 mg Z and 17 mg MZ). Serum carotenoids were quantified at baseline, and at 4 and 8 weeks using HPLC. Response data for normal and AMD subjects were comparable and therefore combined for analysis. We report response as the average of the 4- and 8-week concentrations (saturation plateau). Serum L increased significantly in Group 1 (0·036 μmol/l per mg (269 %); P < 0·001) and Group 2 (0·079 μmol/l per mg (340 %); P < 0·001), with no significant change in Group 3 (0·006 μmol/l per mg (7 %); P = 0·466). Serum Z increased significantly in Group 1 (0·037 μmol/l per mg (69 %); P = 0·001) and Group 2 (0·015 μmol/l per mg (75 %); P < 0·001), with no significant change in Group 3 (- 0·0002 μmol/l per mg (- 6 %); P = 0·384). Serum MZ increased significantly in Group 1 (0·0094 μmol/l (absolute value); P = 0·015), Group 2 (0·005 μmol/l per mg; P < 0·001) and Group 3 (0·004 μmol/l per mg; P < 0·001). The formulation containing all three macular carotenoids (Group 2 supplement) was the most efficacious in terms of achieving the highest combined concentration of the three MP constituent carotenoids in serum, thereby potentially optimising the bioavailability of these compounds for capture by the target tissue (retina).

PMID: 23211762 [PubMed - as supplied by publisher]

J Agric Food Chem. 2012 Dec 3. [Epub ahead of print]

Effect of domestic cooking methods on egg yolk xanthophylls.

Nimalaratne C, Lopes-Lutz D, Schieber A, Wu J.

Abstract: Xanthophylls are a class of bioactive compounds known to play an important role in preventing age related macular degeneration. Egg yolk is a rich source of highly bioavailable xanthophylls inlcluding lutein and zeaxanthin. Effect of domestic cooking methods (boiling, frying, microwaving) on egg yolk xanthophyll content was investigated. A LC-(APCI)-MS/MS method was used to identify and quantify all-E- and Z- isomers of lutein, zeaxanthin, canthaxanthin and β-apo-8'-carotenoic acid ethyl ester in fresh and cooked egg yolks. Both fresh and cooked yolks showed similar xanthophyll profiles but with higher contents of Z- isomers in cooked samples. All-E-lutein was the most affected, with 22.5%, 16.7% and 19.3% reductions in boiled, microwaved and fried yolk extracts respectively. Total xanthophyll losses ranged from 6 to 18%. The results present here could be useful in calculating the dietary intake of xanthophylls and also in assessing the xanthophyll profiles and contents of egg-containing products. KEYWORDS: Egg yolk; Xanthophylls; Domestic cooking methods; LC-(APCI)-MS/MS.

PMID: 23205520 [PubMed - as supplied by publisher]