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MD Research News

Issue 52

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Drug treatment

Curr Drug Discov Technol. 2011 Dec 1. [Epub ahead of print]

Aflibercept (VEGF-TRAP): The Next Anti-VEGF Drug.

Stewart MW.

Department of Ophthalmology, Mayo Clinic Florida, 4500 San Pablo Rd, Jacksonville, FL 32224, USA.

Abstract

The inflammatory cytokine, vascular endothelial growth factor (VEGF), plays a central role in human growth and development, and vascular maintenance. VEGF mediated angiogenesis is essential for tumor growth, as well as exudative age-related macular degeneration, proliferative diabetic retinopathy and retinopathy of prematurity, all of which are characterized by abnormal neovascularization. Ischemia and inflammation also lead to VEGF-mediated breakdown of the blood-retinal barrier, which causes vision diminishing macular edema. To combat these effects, anti-VEGF drugs (antibodies, aptamers, and tyrosine kinase inhibitors) have been developed for both systemic and local (intraocular) use. The next drug to receive regulatory approval will probably be aflibercept (VEGF-Trap), a fusion protein with high VEGF affinity attributed to binding sequences from the native receptors VEGFR1 and VEGFR2. Aflibercept monotherapy significantly reduces tumor growth and extends survival in several orthotropic animal models, and has both prevented and reduced the growth of experimental choroidal neovascularization. Ongoing phase III trials are evaluating the effectiveness of aflibercept combined with chemotherapy in patients with advanced carcinomas. The phase III VELOUR trial determined that patients receiving aflibercept with irinotecan/5-FU as second line chemotherapy for metastatic colorectal cancer experienced extended progression free survival and overall survival. Intravitreal aflibercept improved visual acuity in patients with exudative age-related macular degeneration and was non-inferior to standard therapy (ranibizumab). Ongoing phase III trials are investigating the use of aflibercept for retinal vein occlusions and diabetic macular edema. A regulatory approval application for use in exudative macular degeneration has been filed, with a decision expected by late 2011.

PMID: 21999177 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2011 Oct 19. doi: 10.1111/j.1755-3768.2011.02268.x. [Epub ahead of print]

Predictors of 1-year visual outcome in neovascular age-related macular degeneration following intravitreal ranibizumab treatment.

Bloch SB, la Cour M, Sander B, Hansen LK, Fuchs J, Lund-Andersen H, Larsen M.

Department of Ophthalmology, Glostrup Hospital, Glostrup, Denmark University of Copenhagen, Copenhagen, Denmark.

Purpose: To describe predictors of visual outcome in patients treated with intravitreal ranibizumab for choroidal neovascularisation (CNV) in age-related macular degeneration (AMD).

Methods: Retrospective review of 279 patients with CNV in AMD who fulfilled MARINA/ANCHOR study eligibility criteria and were treated with repeated intravitreal injections of ranibizumab 0.5 mg in routine clinical practice, beginning with three initial injections at 4-week intervals followed by individualized retreatment for the subsequent 9 months. Study parameters included best-corrected visual acuity (BCVA) and morphological characteristics.

Results: Mean BCVA relative to baseline was +4.7 ($p < 0.0001$), +4.2 ($p < 0.0001$)and -0.4 ($p > 0.667$) Early Treatment Diabetic Retinopathy Study letters after 3, 6 and 12 months, respectively, after a mean of 5.1 injections when the proportion of patients with BCVA ≥70 letters had doubled compared with baseline. Predictive factors for BCVA ≤35 letters after 12 months were BCVA ≤35 letters at baseline and month 3 ($p < 0.0001$) while BCVA ≥70 letters at month 12 was associated with BCVA ≥70 letters at baseline and month 3 ($p < 0.001$) and with total lesion size <4 DA ($p = 0.0147$).

Conclusion: Under a ranibizumab regimen with substantially fewer injections than with fixed four-weekly injection regimens, BCVA was improved compared with the natural history of neovascular AMD, but did not achieve the visual gain observed in randomized clinical trials using fixed 4-week retreatment. Visual acuity at month 3, after the initial fixed-interval injections, was the strongest predictor of BCVA at month 12.

PMID: 22008284 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2011 Oct 19. doi: 10.1111/j.1755-3768.2011.02278.x. [Epub ahead of print]

Intravitreal ranibizumab, with or without filter?

Montero JA, Ruiz-Moreno JM, Sanchis-Merino E.

Ophthalmology Unit, Pio del Rio Hortega University Hospital, Valladolid, Spain VISSUM, Alicante Institute of Ophthalmology, Alicante, Spain Ophthalmology Unit, Albacete Medical School, Castilla La Mancha University, Albacete, Spain Pio del Rio Hortega University Hospital, Allergy Unit, Valladolid, Spain.

PMID: 22008393 [PubMed - as supplied by publisher]

Clin Experiment Ophthalmol. 2011 Oct 17. doi: 10.1111/j.1442-9071.2011.02719.x. [Epub ahead of print]

Ranibizumab therapy for choroidal neovascularisation secondary to non-age related macular degeneration causes.

Troutbeck R, Bunting R, van Heerdon A, Cain M, Guymer R.

Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Melbourne, Australia.

Background: To investigate the efficacy of ranibizumab therapy for choroidal neovascular membranes (CNV) secondary to conditions other than macular degeneration. Design: Prospective case series conducted at the Royal Victorian Eye and Ear Hospital. Participants: Twelve month follow-up data for 41 patients with CNV recruited from the outpatient clinic from May 2008 to April 2010 is presented. Fifteen patients had myopia, 7 multifocal choroiditis (MFC) and 8 had other primary causes.

Methods: All patients had visual acuity, fluorescein angiogram and OCT performed at the initial visit (baseline). Ranibizumab was injected with a standard sterile technique. Patients were reviewed after one month and further injections were given at the treating doctors' discretion.

Main Outcome Measures: Change in visual acuity (VA) and central macular thickness (CMT) at 12 months compared to baseline for each of the groups. Local and systemic adverse outcomes were recorded.

Results: Analysis was stratified by primary pathology. On average, 40%, 43% and 25% of patients with myopia, multifocal choroiditis and "other" pathologies, respectively, experienced a 3 or more line improvement in vision. The average number of injections in 12 months was 4.2 for the entire group. CMT significantly decreased in the 12 month period for the combined group ($p = 0.03$). No patient had an adverse systemic side effect, however, there was one case of endophthalmitis.

Conclusions: Ranibizumab is an effective treatment for CNV secondary to non-AMD causes, with most patients gaining an improvement in the first 2 months following injection.

PMID: 22004186 [PubMed - as supplied by publisher]

Med Image Comput Comput Assist Interv. 2011;14(Pt 1):33-40.

Steerable intravitreal inserts for drug delivery: in vitro and ex vivo mobility experiments.

Bergeles C, Kummer MP, Kratochvil BE, Framme C, Nelson BJ.

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Abstract

The progress of wet age-related macular degeneration can now be controlled by intravitreal drug injection. This approach requires repeated injections, which could be avoided by delivering the drug to the retina. Intraocular implants are a promising solution for drug delivery near the retina. Currently, their accurate placement is challenging, and they can only be removed after a vitrectomy. In this paper, we introduce an approach for minimally invasive retinal drug delivery using magnetic intraocular inserts. We briefly discuss the electromagnetic-control system for magnetic implants and then focus on evaluating their ability to move in the vitreous humor. The mobility of magnetic intraocular implants is estimated in vitro with synthesized vitreous humors, and ex vivo with experiments on cadaver porcine eyes. Preliminary results show that with such magnetic implants a vitrectomy can be avoided.

PMID: 22003597 [PubMed - in process]

Am J Ophthalmol. 2011 Oct 17. [Epub ahead of print]

Fixed-Interval Versus OCT-Guided Variable Dosing of Intravitreal Bevacizumab in the Management of Neovascular Age-Related Macular Degeneration: A 12-Month Randomized Prospective Study.

El-Mollayess GM, Mahfoud Z, Schakal AR, Salti HI, Jaafar D, Bashshur ZF.

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

PURPOSE: To compare the efficacy of as-needed or variable dosing of intravitreal bevacizumab to continuous fixed-interval dosing in the management of neovascular age-related macular degeneration (AMD).

DESIGN: Prospective, open-label, randomized clinical study.

METHODS: One hundred twenty eyes of 120 patients with treatment-naïve subfoveal neovascular AMD participated in this study at the American University of Beirut and Hotel Dieu de France Retina Clinics. Eyes were randomized (1:1) to fixed-interval dosing (every 4 to 6 weeks) or variable dosing with intravitreal

bevacizumab (1.25 mg/0.05 mL). Best-corrected visual acuity (BCVA) and central retinal thickness (CRT) using optical coherence tomography (OCT) were measured at baseline and at each follow-up visit. Presence or recurrence of fluid on OCT was the main indicator for retreatment in variable dosing. Main outcome measure was improvement in BCVA and CRT at 12 months.

RESULTS: Compared to baseline, variable dosing had a mean improvement in BCVA of 11.0 letters after 12 months vs 9.2 letters for fixed-interval dosing (P = .81). Similarly, CRT decreased after 12 months by 80.7 μm for variable dosing vs 100.5 μm for fixed-interval dosing (P = .37). The average number of injections over 12 months was higher for fixed-interval dosing than variable dosing (9.5 vs 3.8 injections, P < .001).

CONCLUSIONS: Fixed-interval and variable dosing regimens of intravitreal bevacizumab improved visual acuity and anatomic outcomes after 12 months in eyes with neovascular AMD. However, variable dosing had a reduced treatment burden. Larger trials are needed to confirm these results.

PMID: 22014603 [PubMed - as supplied by publisher]

Curr Eye Res. 2011 Nov;36(11):1005-13.

The impact of subconjunctivally injected EGF and VEGF inhibitors on experimental corneal neovascularization in rat model.

Sener E, Yuksel N, Yildiz DK, Yilmaz B, Ozdemir O, Caglar Y, Degirmenci E.

Ophthalmology Department,Tokat State Hospital , TOKAT , Turkey.

Aim and scope: To investigate the inhibitory effect of subconjunctival application of VEGF antibodies bevacizumab, ranibizumab, pegaptanib, and HER2 antibody trastuzumab on corneal neovascularization in a rat model of experimental corneal neovascularization.

Material and method: Thirty male Wistar albino rats were included in the study. A chemical burn was induced in central cornea of one eye of the rats by a 75% silver nitrate and 25% potassium nitrate stick. Rats were randomly divided into five groups so that each group contained 6 subjects. Right after the chemical burn, 0.1 ml serum physiologic was injected subconjuctivally in control group (group 1). 1.25 mg/0.05 ml bevacizumab was injected in group 2; 1.2 mg/0.1 ml trastuzumab was injected in group 3; 0.5 mg/0.05 ml ranibizumab was injected in group-4; and 0.3 mg/0.1 ml pegaptanib was injected in group 5. On the 8th day of the experiment, rat corneas were photographed by digital photo-camera. Later, eyes of the sacrificed rats were enucleated and corneal speciements were histopathologically analyzed. The percentages of neovascularization on corneal photographs were examined with digital image analysis.

Results: The percentage of corneal neovascularization in all treatment groups was found to be significantly lower than the control group ($p < 0.05$). Bevacizumab was found to be more effective than all other agents ($p < 0.05$). While the degree of inflammation and vascularization in bevacizumab and trastuzumab groups were significantly lower than the control group ($p < 0.05$), the difference was not significant in ranibizumab and pegaptanib groups ($p > 0.05$). In all treatment groups, fibroblast intensity was significantly lower than the control group. In terms of corneal thickness, no significant difference was observed between treatment and control groups ($p > 0.05$).

Conclusion: Bevacizumab, ranibizumab, pegaptanib, and trastuzumab were found effective for the inhibition of corneal NV. In our study we detected that the most effective agent was bevacizumab.

PMID: 21999227 [PubMed - in process]

Arch Soc Esp Oftalmol. 2011 Oct;86(10):335-336. Epub 2011 Sep 9.

Influence of serous macular detachment on the efficacy of ranibizumab treatment in retinal vein occlusions.

[Article in English, Spanish]

Dolz-Marco R, Gallego-Pinazo R, Sanz-Marco E, Díaz-Llopis M, Lleó-Pérez A.

Servicio de Oftalmología, Hospital Universitario y Politécnico La Fe, Valencia, España.

PMID: 22004580 [PubMed - as supplied by publisher]

Insight. 2011 Summer;36(3):20.

Comparison of age-related macular degeneration treatment trial.

American Academy of Ophthalmology.

PMID: 22013648 [PubMed - in process]

BMJ. 2011 Oct 19;343:d6778. doi: 10.1136/bmj.d6778.

Off-label prescribing in macular degeneration.

McCartney M.

PMID: 22012651 [PubMed - in process]

Other treatment & diagnosis

Invest Ophthalmol Vis Sci. 2011 Oct 14. [Epub ahead of print]

Visual Function Tests as Potential Biomarkers in Age-related Macular Degeneration.

Dimitrov PN, Robman LD, Varsamidis M, Aung KZ, Makeyeva GA, Guymer RH, Vingrys AJ.

Center for Eye Research Australia, The University of Melbourne, The Royal Victorian Eye and Ear Hospital, Victoria 3002, Australia.

Purpose: To evaluate the potential of psychophysical assessments of retinal function to provide diagnostic biomarkers of early Age-related Macular Degeneration (AMD).

Methods: Unilateral visual function was assessed in 221 participants (72.86±9.94 years; 67% females) with early AMD (visual acuity better than 20/60) and 109 controls (73.07±10.32 years; 65% females). Psychophysical assessment included steady-state thresholds (4Hz and 14Hz flicker and Red and Blue color) and dynamic tests (Photostress Recovery, PSR and Dark Adaptation, DA). All test-parameters were compared in terms of their diagnostic capacity (sensitivity and specificity), reproducibility and clinical applicability (test-duration and participant's perception of test-difficulty). AMD status was determined according to International Classification and Grading System using digital photography.

Results: All functional measurements were significantly worse, on average, in AMD group compared with controls ($p<0.001$). Static and dynamic parameters showed weak correlations (range, 0.003-0.225). Rod recovery in DA and cone recovery in PSR had the best diagnostic capacity (Receiver Operating Characteristics, AUC, 0.93±0.016 and 0.85±0.021, respectively). Considering diagnostic capacity together with test

reproducibility and clinical applicability the 14 Hz Flicker gave the best outcome followed by PSR. Combination of these two tests was able to detect 71% of abnormal early AMD cases.

Conclusion: All the employed visual function tests had good diagnostic capacity. Combination of the 14Hz flicker thresholds and dynamics of PSR test provided optimal quantitative assessment of retinal functional changes in early AMD, suggesting this set as potentially useful clinical tool to follow progression of early AMD and assess efficacy of interventions.

PMID: 22003115 [PubMed - as supplied by publisher]

Prev Chronic Dis. 2011 Nov;8(6):A147. Epub 2011 Oct 17.

Age-related macular degeneration and smoking cessation advice by eye care providers: a pilot study.

Caban-Martinez AJ, Davila EP, Lam BL, Dubovy SR, McCollister KE, Fleming LE, Zheng DD, Lee DJ.

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Abstract

Smoking is a modifiable risk factor for age-related macular degeneration (AMD), the leading cause of irreversible vision loss in the United States. We conducted a pilot study among eye care providers and AMD patients to assess smoking cessation preferences and cessation services offered at a large academic medical center. Most patients who smoke reported never being advised to quit smoking, although most eye care providers reported that they had advised smokers to quit. Two-thirds of providers expressed a desire for additional training and resources to support patient quit attempts, indicating the need for the integration of smoking cessation opportunities in the clinic setting.

PMID: 22005640 [PubMed - in process]

Acta Med Port. 2011 May;24(3):457-62. Epub 2011 Aug 12.

[Delusional parasitosis associated with dialysis treated with aripiprazole].

[Article in Portuguese]

Duarte C, Choi KM, Li CL.

Serviços de Psiquiatria e de Medicina. Centro Hospitalar Conde de São Januário. Região Administrativa Especial de Macau. República Popular da China.

Abstract

We report the case of a 75-year-old Chinese lady that presented delusional parasitosis with visual hallucinations four months after starting peritoneal dialysis. This psychosis is characterized by the persistent and unshakable belief of being infested with small living organisms, although there is no medical evidence for this. The patient had no previous history of psychiatric disorders, presented diminished visual acuity due to cataracts and macular degeneration, did not show cognitive deterioration, and was medicated with erythropoietin. During the course of the psychosis she presented an episode of visual hallucinations possibly related to Charles Bonnet syndrome. After two months of treatment with aripiprazole the psychotic symptoms remitted considerably. Aripiprazole is a neuroleptic to consider in the treatment of delusional parasitosis.

PMID: 22015035 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2011 Oct 14. [Epub ahead of print]

Central Areolar Choroidal Dystrophy (CACD) and Age-related macular degeneration (AMD): differentiating characteristics in multimodal imaging.

Smailhodzic D, Fleckenstein M, Theelen T, Boon CJ, van Huet RA, van de Ven JP, Den Hollander AI, Schmitz-Valckenberg S, Hoyng CB, Weber BH, Holz FG, Klevering BJ.

Department of Ophthalmology, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.

Purpose: Late-onset central areolar choroidal dystrophy (CACD) may easily be confused with geographic atrophy (GA) in AMD. In order to detect discerning features, the morphological changes in CACD patients and in AMD patients were assessed with confocal scanning laser ophthalmoscopy (cSLO), fundus autofluorescence (FAF) and spectral domain optical coherence tomography (SD-OCT).

Methods: A total of 30 CACD patients with identified PRPH2 gene mutations were analyzed and compared to 19 patients with early AMD and 13 patients with AMD-associated GA, respectively. The presence of drusen and pigment clumping was determined with color fundus photography. High-resolution in vivo imaging was performed with cSLO and SD-OCT (Spectralis HRA+OCT, Heidelberg Engineering, Heidelberg, Germany). FAF images and SD-OCT volume scans were analysed in each study eye.

Results: On FAF, a "speckled" FAF pattern occurred significantly more often in CACD (85%) than in early AMD (5.6%), ($p<0.0001$). There was a significantly higher frequency of sub-RPE deposits in eyes with AMD compared to CACD (36.8% versus 2.1% of scans, $p=0.0019$). Reticular drusen could be visualized by SD-OCT and FAF imaging in 52.6% of the eyes with early AMD and in 100% of the eyes with GA, whereas this drusen phenotype did not manifest in eyes with CACD.

Conclusions: Although outer retinal atrophy is the clinical common feature in advanced CACD as well as GA, there are microstructural alterations on high-resolution SD-OCT and FAF imaging, which allow for the differentiation between CACD and AMD. The findings may help to identify patients where a diagnostic PRPH2 screening is warranted.

PMID: 22003107 [PubMed - as supplied by publisher]

Exp Mol Pathol. 2011 Oct 6. [Epub ahead of print]

Serum autoantibody biomarkers for age-related macular degeneration and possible regulators of neovascularization.

Morohoshi K, Patel N, Ohbayashi M, Chong V, Grossniklaus HE, Bird AC, Ono SJ.

Division of Allergy and Immunology, Department of Pediatrics, Cincinnati Children's Hospital, Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, USA; Department of Ophthalmology, Emory University School of Medicine and Emory Eye Center, Dobbs Ocular Immunology Laboratories, Atlanta, GA, USA.

Abstract

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in industrial countries. Its pathogenesis is at least partially mediated by immunological factors, including a possible autoimmune response. To date, only a few antibodies have been identified in sera from patients with AMD. In order to reveal an autoantibody profile for AMD and identify biomarkers for progression of this disease, we have performed an antigen microarray analysis of serum samples from patients with AMD and healthy controls. Sera from the AMD groups contained high levels of IgG and IgM autoantibodies to some systemic antigens when compared to the normal group. Targeted antigens included cyclic nucleotide phosphodiesterase, phosphatidylserine (PS) and proliferating cell nuclear antigen. The IgG/IgM ratio for antibodies to

PS was notably elevated in the AMD group compared to the normal group, and this ratio correlated best with the stage of AMD patients with an anti-PS ratio greater than the cut-off value had a 44-fold risk for advanced AMD with choroidal neovascularization. PS immunoreactivity was also elevated in AMD retina. Moreover, IgG autoantibodies purified from sera of AMD patients induced more tube formation on choroidal -retinal endothelial cells compared to those of healthy donors. Hence, sera from patients with AMD contain specific autoantibodies which may be used as biomarkers for AMD, and the IgG/M ratio for autoantibodies to PS might allow better monitoring of AMD progression.

PMID: 22001380 [PubMed - as supplied by publisher]

Retina. 2011 Oct 18. [Epub ahead of print]

Gas-Assisted Release of Vitreomacular Adhesion in Wet Age-Related Macular Degeneration.

Kim YM, Lee SJ, Koh HJ.

*The Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, Seoul, Korea †Department of Ophthalmology, Dongguk University Ilsan Hospital, Dongguk University, Seoul, Korea.

PMID: 22012205 [PubMed - as supplied by publisher]

Pathogenesis

Rejuvenation Res. 2011 Oct 18. [Epub ahead of print]

5'-Adenosine Monophosphate-Activated Protein Kinase-Mammalian Target of Rapamycin Axis As Therapeutic Target for Age-Related Macular Degeneration.

Hyttinen JM, Petrovski G, Salminen A, Kaarniranta K.

Department of Ophthalmology, Institute of Clinical Medicine, University of Eastern Finland , Kuopio, Finland .

Abstract:

Age-related macular degeneration (AMD) is the most common reason for blindness in developed countries. AMD essentially involves chronic oxidative stress, increased accumulation of lipofuscin in retinal pigment epithelial (RPE) cells, and extracellular drusen formation, as well as presence of chronic inflammation in the retina. The capacity to prevent the accumulation of cellular cytotoxic protein aggregates is decreased in senescent cells, which may evoke lipofuscin accumulation into lysosomes in postmitotic RPE cells. The formation of lipofuscin, in turn, decreases the lysosomal enzyme activity and impairs the autophagic clearance of damaged proteins destined for cellular removal. 5'-Adenosine monophosphate-activated protein kinase (AMPK) is a well-known inhibitor of mammalian target of rapamycin (mTOR) that subsequently evokes induction of autophagy. This review examines the novel potential therapeutic targets on the AMPK-mTOR axis and the ways in which autophagy clearance can suppress or prevent RPE degeneration and development of AMD.

PMID: 22007913 [PubMed - as supplied by publisher]

Epidemiology

Ned Tijdschr Geneeskd. 2011;155(41):A3461.

[Increase in the demand for eye-care services in the Netherlands 2010-2020].

[Article in Dutch]

Keunen JE, Verezen CA, Imhof SM, van Rens GH, Asselbergs MB, Limburg JJ.

Source

UMC St. Radboud, Instituut voor Oogheelkunde, Nijmegen.

OBJECTIVE: The demand for eye-care services in the Netherlands is increasing. This article indicates the causes and attempts to provide an estimate of the increase between 2010 and 2020 and to indicate what will be the consequences.

DESIGN: Descriptive study.

METHOD: In the absence of data on the numbers of blind and visually impaired people in the Netherlands, we used data from the records of general practitioners, yearly statistics for the number of relevant activities in hospitals and a mathematical model to calculate the number of blind and visually impaired in the Netherlands. The data mentioned were extrapolated to the population of 2020. Additionally, the expected number of new treatments of neovascular age-related macular degeneration (AMD) and macular oedema in diabetic retinopathy and retinal venous occlusion were calculated by a model.

RESULTS: The number of people over 65 in the Netherlands increases by 34% between 2010 and 2020. The registrations by general practitioners show an increase of 43% of patients with eye conditions. Modelling of the new treatment methods demonstrates a threefold increase of the number of treatments. Finally, it appears that the number of blind and visually impaired people increases by 20%. The prevalence of visual impairment is the highest in elderly in health-care institutions, mentally handicapped and elderly living independently.

CONCLUSION: The demand for eye-care services will increase by 200-300% between 2010 and 2020. The most important cause for this is the new treatment for 'wet' AMD and macular oedema using intravitreal angiogenesis inhibitors. The capacity of eye care services needs to be increased, partly by a redistribution of tasks between different professional groups within the eye care sector. Routine vision screening of elderly in care institutions and people with a mental handicap can reduce the number of Dutch people with avoidable visual impairment. For elderly living independently, provision of information and selective screening is indicated.

PMID: 22008156 [PubMed - in process]

Genetics

Invest Ophthalmol Vis Sci. 2011 Oct 14. [Epub ahead of print]

Complement factor D in age-related macular degeneration.

Stanton CM, Yates JR, den Hollander AI, Seddon JM, Swaroop A, Stambolian D, Fauser S, Hoyng C, Yu Y, Atsuhiro K, Branham K, Othman M, Chen W, Kortvely E, Chalmers K, Hayward C, Moore AT, Dhillon B, Ueffing M, Wright AF.

MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, Edinburgh EH4 2XU, UK;

Purpose: To examine the role of complement factor D (CFD) in age-related macular degeneration (AMD) by analysis of genetic association, copy number variation and plasma CFD concentrations.

Methods: Single nucleotide polymorphisms (SNPs) in the CFD gene were genotyped and the results analysed by binary logistic regression. CFD gene copy number was analysed by Taqman(®) gene copy number assay. Plasma CFD was measured by an enzyme-linked immunosorbent assay.

Results: Genetic association was found between CFD gene SNP rs3826945 and AMD (odds ratio 1.44, p=0.028) in a small discovery case-control series (462 cases and 325 controls) and replicated in a combined cohorts meta-analysis of 4765 cases and 2693 controls, with an odds ratio of 1.11 (p=0.032), with the association almost confined to females.Copy number variation in the CFD gene was identified in 13 out of 640 samples examined but there was no difference in frequency between AMD cases (1.3%) and controls (2.7%).Plasma CFD concentration was measured in 751 AMD cases and 474 controls and found to be elevated in AMD cases (p=0.00025). The odds ratio for those in the highest versus lowest quartile for plasma CFD was 1.81. The difference in plasma CFD was again almost confined to females.

Conclusions: CFD regulates activation of the alternative complement pathway, which is implicated in AMD pathogenesis. We found evidence for genetic association between a CFD gene SNP and AMD and a significant increase in plasma CFD concentration in AMD cases compared with controls, consistent with a role for CFD in AMD pathogenesis.

PMID: 22003108 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2011 Oct 14. [Epub ahead of print]

Association of Elastin Gene Polymorphism to Age-related Macular Degeneration and Polypoidal Choroidal Vasculopathy.

Yamashiro K, Mori K, Nakata I, Tsuchihashi T, Horie-Inoue K, Nakanishi H, Tsujikawa A, Saito M, Iida T, Yamada R, Matsuda F, Inoue S, Awata T, Yoneya S, Yoshimura N.

Department of Ophthalmology, Kyoto University Graduate School of Medicine, Kyoto, Japan;

Purpose: To see if there is an association in Japanese between elastin gene polymorphisms and neovascular age-related macular degeneration (AMD) or its subtypes: typical AMD (tAMD) and polypoidal choroidal vasculopathy (PCV).

Methods: We genotyped five single nucleotide polymorphisms (SNPs), rs2301995, rs2856728, rs868005, rs884843, and rs13239907, at Kyoto University and Saitama Medical University. A case-control study was performed on 1296 patients with AMD and 478 controls.

Results: A statistically significant association was detected between the rs2301995 SNP and AMD (P = 0.018). Furthermore, subtype analysis revealed a significant association of rs2301995 with tAMD (P = 0.0018), but not with PCV. The genotype distribution of rs2301995 also differed significantly between tAMD and PCV (P = 0.00030). The trend in genotype distribution of rs2301995 was similar between the Kyoto and the Saitama studies. The A allele frequency was higher in tAMD while it was similar in PCV and in controls, which is opposite to a previous report that A allele frequency is higher in PCV while it is similar in tAMD and in controls. Haplotype analysis also showed that elastin gene polymorphism is significantly associated with tAMD (P = 0.0055), but not with PCV.

Conclusions: The elastin gene is associated with AMD in Japanese. Furthermore, our findings suggest that the elastin gene is a susceptibility gene for tAMD but not for PCV, which is opposite to a previous report that the elastin gene is the susceptibility gene for PCV but not for tAMD.

PMID: 22003121 [PubMed - as supplied by publisher]

Arch Soc Esp Oftalmol. 2011 Oct;86(10):327-330. Epub 2011 Jul 19.

X linked retinoschisis, unusual presentation: strabismus.

[Article in English, Spanish]

Areizaga Osés AB, Martínez Fernández R, Galdos Iztueta M, Muruzabal Zaldíbar N.

Unidad de Oftalmología,Hospital San Eloy, Baracaldo, Vizcaya, España.

CASE REPORT: X linked retinoschisis is a recessively inherited degenerative retinopathy. We report two cases that debuted with an unusual presentation (strabismus) in early childhood (months). Both of them presented with vitreous veils in the retinal periphery. Mutation in the XLRS1 gene was detected in both cases.

DISCUSSION: X linked retinoschisis is one of the leading causes of macular degeneration in male children. Clinical features include a stellate foveal schisis, with or without peripheral retinoschisis. Clinical diagnosis is often difficult because of a high degree of phenotype variability. Furthermore, ERG and OCT may be normal in early stages of the disease. In our opinion, the XLRS1 gene mutation screening provides a powerful clinical tool for evaluating clinically ambiguous cases of X linked retinoschisis.

PMID: 22004578 [PubMed - as supplied by publisher]

Diet

Eur J Ophthalmol. 2011 Oct 17:0. doi: 10.5301/ejo.5000069. [Epub ahead of print]

Carotenoids in Age-related Maculopathy Italian Study (CARMIS): two-year results of a randomized study.

Piermarocchi S, Saviano S, Parisi V, Tedeschi M, Panozzo G, Scarpa G, Boschi G, Lo Giudice G; for The Carmis Study Group.

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Purpose: The high concentration of carotenoids in the macula, plus evidence linking oxidative stress to age-related macular degeneration (AMD) and carotenoids to antioxidation, generated the hypothesis that higher antioxidant intakes can prevent AMD. The aim of this study was to determine whether nutritional supplementation with a targeted nutritional supplement improves visual acuity and visual function in AMD.

Methods: In this multicenter, prospective open-label randomized study, 145 patients were randomly assigned to 2 different treatment groups. Interventions were lutein (10 mg), zeaxanthin (1 mg), astaxanthin (4 mg; AZYR SIFI, Catania, Italy), and antioxidants/vitamins supplementation formula or no dietary supplementation for 2 years. Primary outcome was mean changes in visual acuity (VA) at 12 and 24 months. Other measures included contrast sensitivity (CS) and National Eye Institute visual function questionnaire (NEI VFQ-25) scores at 12 and 24 months.

Results: Patients in the treated group showed stabilization of VA with significantly (p=0.003) better VA scores (81.4±7.2) compared to the nontreated group (76.8±8.9) at 24-month follow-up. An improvement in CS (p=0.001) and final mean NEI VFQ-25 composite scores at 12 and 24 months higher in treated group compared to nontreated group were also shown (p<0.001).

Conclusions: Patients treated with lutein/zeaxanthin and astaxanthin together with other nutrients were more likely to report clinically meaningful stabilization/improvements in VA, CS, and visual function through 24 months compared with nontreated subjects. Further studies are needed with more patients and for longer periods of time.

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