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Drug treatment

J Ophthalmol. 2012;2012:637316. Epub 2012 Feb 9.

New Approach of Anti-VEGF Agents for Age-Related Macular Degeneration.

Park YG, Rhu HW, Kang S, Roh YJ.

Department of Ophthalmology, Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea, No. 62 Yeouido-dong, Yeongdeungpo-gu, Seoul 150-713, Republic of Korea.

Abstract

Age-related macular degeneration (AMD) is the leading cause of visual loss in older population. Angiogenesis is an important factor associated with the development of CNV due to AMD. Treatment of CNV with intravitreal anti-VEGF monotherapy is currently the standard of care. However, not all patients respond to monotherapy, and modified anti-VEGF treatment regimen and combination therapy may target reducing treatment frequency or improving visual outcome. This paper reviews the many clinical trials that have been performed utilizing several treatment regimens. While many trials have shown that this variable therapy is justifiable, further study is required to determine correct regimens and dosage.

PMID: 22496964 [PubMed - in process] PMCID: PMC3307057

Retina. 2012 Apr 10. [Epub ahead of print]

INTRAVITREAL INJECTION OF RANIBIZUMAB DURING CATARACT SURGERY IN PATIENTS WITH DIABETIC MACULAR EDEMA.

Rauen PI, Ribeiro JA, Almeida FP, Scott IU, Messias A, Jorge R.

*Department of Ophthalmology, Otorhinolaryngology and Head and Neck Surgery, School of Medicine of Ribeirão Preto, University of São Paulo, Ribeirão Preto, Brazil †Departments of Ophthalmology and Public Health Sciences, Penn State College of Medicine, Hershey, PA.

PURPOSE: To investigate macular thickness and visual acuity changes after 1 intravitreal injection of 0.5-mg ranibizumab during phacoemulsification cataract surgery in eyes with diabetic macular edema refractory to laser treatment.

METHODS: Eleven eyes of 11 patients with diabetic macular edema refractory to modified Early Treatment Diabetic Retinopathy Study laser therapy received intravitreal during phacoemulsification cataract surgery.

Comprehensive ophthalmic evaluation was performed preoperatively and at 1, 4, 8 ± 1, and 12 ± 2 weeks postoperatively. Main outcome measures included central subfield thickness and best-corrected Early Treatment Diabetic Retinopathy Study visual acuity.

RESULTS: Eleven patients completed the 12-week study visit. Mean central subfield thickness (±SEM) was 399.82 ± 29.50 μm at baseline and did not change significantly at any postoperative study visit (P > 0.05). Mean (±SEM) best-corrected Early Treatment Diabetic Retinopathy Study visual acuity was 0.95 ± 0.13 logarithm of the minimum angle of resolution (20/200) at baseline and was significantly improved at Weeks 1 (0.38 ± 0.13), 4 (0.38 ± 0.11), 8 (0.35 ± 0.08), and 12 (0.46 ± 0.12) after treatment (P < 0.05).

CONCLUSION: In this case series of patients with diabetic macular edema refractory to laser therapy, intravitreal ranibizumab administered during cataract surgery was associated with no significant change in central subfield thickness postoperatively. Significant improvement in best-corrected Early Treatment Diabetic Retinopathy Study visual acuity was observed after treatment, likely because of cataract removal.

PMID: 22495327 [PubMed - as supplied by publisher]

J Pharmacol Exp Ther. 2012 Apr 11. [Epub ahead of print]

Polyethylene glycol modified pigment epithelial-derived factor: new prospects for treatment of retinal neovascularization.

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Abstract

Pathological retinal neovascularization and choroidal neovascularization are major causes of vision loss in a variety of clinical conditions, such as retinopathy of prematurity (ROP), age-related macular degeneration, and diabetic retinopathy. Pigment epithelial-derived factor (PEDF) has been found to be the most potent endogenous nature inhibitor of neovascularization. However, the application of PEDF is restricted due to the unstable and short half-life property. Polyethylene glycol (PEG) has been used as a drug carrier to slow clearence rate for decades. The present study investigated PEGylated-PEDF for the first time, and evaluated its long-term effects on preventing angiogenesis in vitro and in vivo. PEG showed lower cytotoxicity to the human umbilical vein endothelial cells (HUVEC). In vitro, PEGylated-PEDF inhibited HUVEC proliferation, migration, tube formation, vacular endothelium growth factor (VEGF) secretion, induced HUVEC apoptosis in a dose-dependece maner, and had statistically significant difference comparing to PEDF treatmet group. In vivo, PEGylated-PEDF had a long lasting effect both in plasma and retina concentration. In oxygen-induced retinopathy (OIR) model, once intravitreous injection of PEGylated-PEDF after remove pups into room air, showed significant diffrence in inhibition of retina neuvascularization, which decreased non-perfusion area comparing to PEDF teated group. Our present study demonstrated the long-term inhibitory effect of PEGylated-PEDF on the prevention of neovascularization in vitro and in vivo for the first time. These data suggest that PEGylated-PEDF could offer a innovative therapeutic strategy for preventing retinal neovascularization.

PMID: 22495066 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2012 Apr 11. [Epub ahead of print]

[Anti-VEGF Therapy for Neovascular Age-Related Macular Degeneration: Therapeutic Strategies.]

[Article in German]

Aktuelle Stellungnahme der Retinologischen Gesellschaft,; der Deutschen Ophthal-mologischen Gesellschaft; und des Berufsverbands der Augenärzte Deutschlands e. V..

PMID: 22495357 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2012 Apr;229(4):451-453. Epub 2012 Apr 11.

Intravitreal Administration of Ranibizumab for Idiopathic Choroidal Neovascularization in a Pregnant Woman.

Sarhianaki A, Katsimpris A, Petropoulos IK, Livieratou A, Theoulakis PE, Katsimpris JM.

Department of Obstetrics and Gynaecology, General Hospital of Patras "Agios Andreas", Patras, Greece.

PMID: 22496030 [PubMed - as supplied by publisher]

Ocul Surf. 2012 Apr;10(2):67-83. Epub 2012 Jan 25.

Corneal neovascularization and the utility of topical VEGF inhibition: ranibizumab (lucentis) vs bevacizumab (avastin).

Stevenson W, Cheng SF, Dastjerdi MH, Ferrari G, Dana R.

Schepens Eye Research Institute, Massachusetts Eye & Ear Infirmary, Harvard Medical School, Boston, MA, USA.

Abstract

Corneal avascularity is necessary for the preservation of optimal vision. The cornea maintains a dynamic balance between pro- and antiangiogenic factors that allows it to remain avascular under normal homeostatic conditions; however, corneal avascularity can be compromised by pathologic conditions that negate the cornea's "angiogenic privilege." The clinical relevance of corneal neovascularization has long been recognized, but management of this condition has been hindered by a lack of safe and effective therapeutic modalities. Herein, the etiology, epidemiology, pathogenesis, and treatment of corneal neovascularization are reviewed. Additionally, the authors' recent findings regarding the clinical utility of topical ranibizumab (Lucentis(®)) and bevacizumab (Avastin(®)) in the treatment of corneal neovascularization are summarized. These findings clearly indicate that ranibizumab and bevacizumab are safe and effective treatments for corneal neovascularization when appropriate precautions are observed. Although direct comparisons are not conclusive, the results suggest that ranibizumab may be modestly superior to bevacizumab in terms of both onset of action and degree of efficacy. In order to justify the increased cost of ranibizumab, it will be necessary to demonstrate meaningful treatment superiority in a prospective, randomized, head-to-head comparison study.

PMID: 22482468 [PubMed - in process]

Acta Ophthalmol. 2012 Apr 10. doi: 10.1111/j.1755-3768.2012.02421.x. [Epub ahead of print]

Incidence of Charles Bonnet syndrome after intravitreal bevacizumab injection in neovascular age-related macular degeneration.

Zhang H, Liu ZL, Sun P, Gu F.

Department of Ophthalmology, the First Hospital of China Medical University, Shenyang, China.

PMID: 22490079 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2012 Apr;229(4):447-450. Epub 2012 Apr 11.

Coats Disease in a 14-year-Old Boy Treated with Intravitreal Ranibizumab and Retinal Laser Photocoagulation.

Theoulakis PE, Halki A, Petropoulos IK, Katsimpris JM.

Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom.

PMID: 22496029 [PubMed - as supplied by publisher]

Other treatment & diagnosis

J Phys Chem B. 2012 Apr 9. [Epub ahead of print]

Subsurface Femtosecond Tissue Alteration: Selectively Photobleaching Macular Degeneration Pigments in Near Retinal Contact.

Manevitch Z, Lewis A, Levy C, Zeira E, Banin E, Manevitch A, Khatchatouriants A, Pe'er J, Galun E, Hemo I.

Abstract

This paper uses advances in the manipulation of light to address a general clinical manifestation associated with a variety of clinical disorders. These disorders require subsurface tissue manipulation with ultralow collateral damage. Examples are age related macular degeneration (AMD), fungal infections, tumors surrounded by overlying tissue etc. Lasers have revolutionized the use of light in clinical settings but most lasers used in medicine cannot address such problems of depth selective tissue manipulation since one photon based laser tissue interactions provide a cone of excitation where the energy density is sufficiently high to excite heat or fluorescence in the entire cone. Thus, it is difficult to excite a specific depth of a tissue without affecting the overlying surface. However, the advent of femtosecond (fsec) lasers have caused a revolution in multiphoton microscopy(1,2) and fabrication (3). With such lasers the photon energy density is only high enough for such multiphoton processes in the focal volume and this opens a new direction to address subsurface tissue manipulation. Here we show in an AMD animal model, Ccr2 KO knockout mutant mice, non-invasive, selective fsec two photon photobleaching of pigments associated with AMD that accumulate under and in ultra close proximity of the overlying retina. Pathological evidence is presented that indicates the lack of collateral damage to the overlying retina or other surrounding tissue.

PMID: 22482826 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2012 Apr;229(4):399-402. Epub 2012 Apr 11.

Multimodal Imaging of Autosomal Dominant Drusen.

Zweifel SA, Maygar I, Berger W, Tschuor P, Becker M, Michels S.

Department of Ophthalmology, University Hospital Zurich, Zurich, Switzerland.

Background: Malattia Leventinese (ML) is a dominantly inherited macular dystrophy characterized by a radial pattern of drusen in the macular area and on the nasal edge of the optic disc. This case series describes the morphological features of drusen associated with ML using multimodal imaging.

History and Signs: Three patients (two of the same family but only one with the ML phenotype) were analyzed by multimodal imaging including spectral domain optical coherence tomography (SD OCT) and genetic testing. In two patients multiple drusen in the macular region and around the optic nerve head were

observed bilaterally. A radial pattern was only seen in one patient. These drusenoid deposits showed early hyperfluorescence in fluorescein angiography (FA) and intense staining in indocyanine green angiography similar to cuticular drusen (basal laminar drusen). The corresponding SD OCT scan revealed two types of deposits. The first, more prominent type, were focal nodular sub-retinal pigment epithelium (RPE) deposits. The second type of deposit appears to be localized on the anterior part of the RPE comparable to subretinal drusenoid deposits (SDD; reticular pseudodrusen).

Therapy and Outcome: A single nucleotide variation c.1033C>T (p.R345 W) in the EFEMP1 gene was found in case 1 (classic ML), but could not be detected in case 2 and 3. So far our patients have not suffered from any visual complaints and have not developed choroidal neovascularization. They will be followed up regularly.

Discussion: Multimodal imaging including SD OCT provided new information about the appearance of drusen in eyes with ML/early onset drusen. In addition to the sub-RPE deposits some deposits appear above the RPE, however have different characteristic findings on FA/ICG, autofluorescence, near infrared reflectance and blue light imaging than SDD observed in patients with age-related macular degeneration. SD OCT alone might not be sufficient to characterize these type of drusen in ML.

PMID: 22496012 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2012 Apr 12. [Epub ahead of print]

Differential Optical Density of Subretinal Spaces.

Neudorfer M, Weinberg A, Loewenstein A, Barak A.

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PURPOSE: To investigate the optical density characteristics of subretinal spaces in neovascular age-related macular degeneration (AMD), diabetic retinopathy (DR), rhegmatogenous retinal detachment (RRD), central serous retinopathy (CSR), retinoschisis (RS) and pseudophakic cystoids macular edema (PCME).

METHODS: Patients in whom subretinal fluid (SRF) was detected by optical coherence tomography (OCT; SPECTRALIS, SD-OCT, Heidelberg Engineering), and whose earliest OCT scans showed sufficient SRF for sampling that did not include tissue edges, were chosen for study. The highest quality B-Scan containing SRF (as graded by the OCT image acquisition software) was analyzed. Optical density measurements were obtained using ImageJ, an open code Java-based image processing software.

RESULTS: The diagnoses of the 71 patients who met the inclusion criteria were AMD in 17, DR in 7, RRD in 18, CSR in 17, RS in 8 and PCME in 4. Optical density ratios (ODRs) were calculated as SRF OD divided by vitreous OD. ODRs were significantly higher in patients with AMD, DR, CSR, and PCME than those with RRD and RS. No significant difference in vitreous reflectivity was detected between the former and the latter patients.

CONCLUSIONS: The finding that disease states produce significant changes in optical density ratios calls for further investigation of the possible usefulness of the parameter in differentiating between disease states, in determining the outcome of various retinal diseases, and in designing therapies aimed at treating the disease by correcting the abnormal density.

PMID: 22499985 [PubMed - as supplied by publisher]

Medicina (Kaunas). 2012 Apr 5;48(2). [Epub ahead of print]

Quality of Life in Patients With Age-Related Macular Degeneration.

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Abstract

The aim of this study was to evaluate the quality of life in persons affected by age-related macular degeneration. MATERIAL AND METHODS. The study was performed in the Clinic of Ophthalmology, Hospital of Lithuanian University of Health Sciences. A total of 140 patients completed the Visual Functioning Questionnaire and the Hospital Anxiety and Depression Scale (HADS) during this prospective study. The patients were divided into two groups: patients with age-related macular degeneration (70 patients) and control patients (70 patients). RESULTS. There was a significant difference in the quality of life between groups (P<0.0001). Analyzing patients with age-related macular degeneration within the group (patients with monocular or binocular disorders), significant differences in near vision (P=0.003), far vision (P=0.04), color vision (P=0.01), and social functioning (P=0.02) were observed. Mental health (r=0.326, P=0.02), dependency (r=0.340, P=0.02), and role difficulties (r=0.355, P=0.01) were found to be significantly associated with general vision in the age-related macular degeneration group. CONCLUSIONS. Age-related macular degeneration appeared to have a great impact on the quality of life. General vision impairment caused by age-related macular degeneration affects patient's mental health, dependency, and role difficulties.

PMID: 22491386 [PubMed - as supplied by publisher]

Zhonghua Yan Ke Za Zhi. 2012 Feb;48(2):103-5.

[Correctly evaluate the role of visual acuity in age-related macular degeneration treatment].

[Article in Chinese]

Zhang F.

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Abstract

Age-related macular degeneration (AMD) is the leading cause of irreversible visual loss in aged population. As the aging of population, the prevalence of AMD increases gradually. Anti-VEGF medication intravitreal injection, which can obtain good therapeutic efficiency and is relatively safe, becomes the main therapy for neovascular AMD. However, high-frequency repeated treatment increases the intravitreal injections risk, as well as the costs. In clinical practice, to pursue the best-corrected visual acuity, high-frequency repeated injections are implemented and inflict psychological pressure and economic burden on patients. The author believes that to pursue the best corrected visual acuity is the ultimate aim but not the only one for every ophthalmologist and patient. The activity of lesions should be overall evaluated with fundus imaging technologies. Being people-oriented is the principle in clinical medicine. A treatment plan is made according to the patients' sickness and economy and to coordinate the relation between the best corrected visual acuity and the numbers of treatment. Based on the stabilized lesion, patient should be benefited at the lowest risk and cost with the best effect.

PMID: 22490943 [PubMed - in process]

Pathogenesis

Nat Med. 2012 Apr 8. doi: 10.1038/nm.2717. [Epub ahead of print]

NLRP3 has a protective role in age-related macular degeneration through the induction of IL-18 by drusen components.

Doyle SL, Campbell M, Ozaki E, Salomon RG, Mori A, Kenna PF, Farrar GJ, Kiang AS, Humphries MM, Lavelle EC, O'Neill LA, Hollyfield JG, Humphries P.

1] School of Biochemistry and Immunology, Trinity Biomedical Sciences Institute, Trinity College Dublin, Dublin 2, Ireland. [2].

Abstract

Age-related macular degeneration (AMD) is the leading cause of central vision loss worldwide. Drusen accumulation is the major pathological hallmark common to both dry and wet AMD. Although activation of the immune system has been implicated in disease progression, the pathways involved are unclear. Here we show that drusen isolated from donor AMD eyes activates the NACHT, LRR and PYD domains-containing protein 3 (NLRP3) inflammasome, causing secretion of interleukin-1β (IL-1β) and IL-18. Drusen component C1Q also activates the NLRP3 inflammasome. Moreover, the oxidative-stress-related protein-modification carboxyethylpyrrole (CEP), a biomarker of AMD, primes the inflammasome. We found cleaved caspase-1 and NLRP3 in activated macrophages in the retinas of mice immunized with CEP-adducted mouse serum albumin, modeling a dry-AMD-like pathology. We show that laser-induced choroidal neovascularization (CNV), a mouse model of wet AMD, is exacerbated in Nlrp3(-/-) but not Il1r1(-/-) mice, directly implicating IL-18 in the regulation of CNV development. These findings indicate a protective role for NLRP3 and IL-18 in the progression of AMD.

PMID: 22484808 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2012 Apr 10. doi: 10.1111/j.1755-3768.2012.02414.x. [Epub ahead of print]

Cytokine concentration in aqueous humour of eyes with exudative age-related macular degeneration.

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Purpose: To measure the concentration of cytokines in the aqueous humour of eyes with exudative age-related macular degeneration (AMD).

Methods: The clinical interventional study included a study group of 18 patients with exudative AMD and a control group of 20 patients undergoing routine cataract surgery. Age did not vary significantly ($p = 0.36$) between study group (80.8 ± 6.4 years) and control group (77.0 ± 9.9 years), nor did gender ($p = 0.75$). During the interventions, aqueous humour samples were obtained, in which the concentration of cytokines was measured using a solid-phase chemiluminescence immunoassay. Macular thickness was measured by optical coherence tomography (OCT).

Results: In the study group as compared to the control group, significantly higher concentrations were measured for epithelial growth factor (EGF) ($p = 0.017$), human growth factor (HGF) ($p = 0.048$), intercellular adhesion molecule-1 (ICAM1) ($p = 0.028$), interleukin 12p40 (IL12p40) ($p = 0.009$), interleukin 1a2 (IL1a2) ($p = 0.01$), interleukin 3 (IL3) ($p = 0.02$), interleukin 6 (IL6) ($p = 0.006$), interleukin 8 (IL8) ($p = 0.02$), monocyte chemoattractant protein-1 (MCP-1) ($p = 0.048$), monokine

induced by interferon gamma (MIG) (p = 0.016), matrix metalloproteinase 9 (MMP9) (p = 0.004) and plasminogen activator inhibitor 1 (PAI1) (p = 0.006). Macular thickness was significantly associated with the concentrations of EGF (p = 0.001), HGF (p = 0.02), ICAM1 (p = 0.001), interleukin 12p40 (p = 0.006), IL 1a2 (p = 0.002), MIG (p = 0.001), MMP9 (p < 0.001) and PAI1 (p = 0.01). Interleukin 6 and MCP-1 showed significant associations with the height of retinal pigment epithelium detachment.

Conclusions: Numerous cytokines are associated with the presence and the amount of exudative AMD.

PMID: 22490043 [PubMed - as supplied by publisher]

J Biomed Mater Res A. 2012 Apr 10. doi: 10.1002/jbm.a.34021. [Epub ahead of print]

Cell-adhesive thermogelling PNIPAAm/hyaluronic acid cell delivery hydrogels for potential application as minimally invasive retinal therapeutics.

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Abstract

Copolymers of N-isopropylacrylamide (NIPAAm) and acrylic acid N-hydroxysuccinimide (NAS) were synthesized via free radical polymerization and conjugated with amine-functionalized hyaluronic acid (HA) and cell adhesive RGDS peptides. These novel copolymers were designed to facilitate noninvasive delivery of a liquid suspension of cells into the delicate subretinal space for treatment of retinal degenerative diseases such as age-related macular degeneration (AMD) and diabetic retinopathy. The various synthesized copolymers all displayed subphysiological phase transition temperatures, thereby allowing temperature-induced scaffold formation and subsequent entrapment of transplanted cells within an adhesive support matrix. Successful grafting of HA and RGDS peptides were confirmed with Fourier Transform Infrared (FTIR) spectroscopy and quantified with (1) H Nuclear Magnetic Resonance (NMR) spectroscopy. All copolymers demonstrated excellent compatibility with retinal pigment epithelial (RPE) cells in culture and minimal host response was observed following subcutaneous implantation into hairless SKH1-E mice (strain code 447).

PMID: 22492502 [PubMed - as supplied by publisher]

Adv Biochem Eng Biotechnol. 2012 Apr 11. [Epub ahead of print]

RNA Aptamers: A Review of Recent Trends and Applications.

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Abstract

RNA aptamers, small oligonucleotides derived by an in-vitro selection process called SELEX (Systematic Evolution of Ligands by EXperimental enrichment), are important candidates for therapeutic and diagnostic applications. RNA aptamers have high affinity and specificity for their target molecules. In this review, we describe methods for generating RNA aptamers (the SELEX technique and modified SELEX processes) and therapeutic applications for diseases such as neovascular age-related macular degeneration (AMD), inflammatory diseases, and obesity. We also analyze the social networks among researchers and organizations (universities, research institutes, firms, etc.) that are active in the pursuit of aptamer-based

therapeutic approaches. This study provides relevant information on recent research trends in RNA aptamers.

PMID: 22491855 [PubMed - as supplied by publisher]

Epidemiology

Br J Ophthalmol. 2012 Apr 4. [Epub ahead of print]

Risk of selected eye diseases in people admitted to hospital for hypertension or diabetes mellitus: record linkage studies.

Goldacre MJ, Wotton CJ, Keenan TD.

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AIMS: Associations among hypertension, diabetes mellitus and some ophthalmic diseases are well established; associations with others are more equivocal. The aim was to quantify associations accurately using large epidemiological datasets.

METHODS: Analysis of the Oxford Record Linkage Study (ORLS), 1963-1998, and English linked hospital episode statistics (LHES), 1999-2010; calculation of rate ratios of eye disease in a hypertension cohort and a diabetes cohort, compared with a reference cohort as control.

RESULTS: Risk of cataract following hypertension was marginally elevated (rate ratio ORLS 1.15, 95% CI 1.00 to 1.31; LHES 1.06, 1.01 to 1.10), as was risk of glaucoma (LHES 1.07, 1.00 to 1.14) and age-related macular degeneration (AMD) (LHES 1.14, 1.02 to 1.27). Risk of retinal vein or artery occlusion was elevated three- to fivefold in both populations. Risk of retinal detachment was elevated in LHES at 1.52 (1.43 to 1.73). Risk of cataract in diabetes was high in ORLS and LHES at, respectively, 2.95 (2.75 to 3.16) and 2.30 (2.24 to 2.35), as was risk of glaucoma: 2.47 (2.14 to 2.84) and 2.23 (2.15 to 2.30). Risks were high for AMD (10.3, 8.1 to 13.1, and 3.46, 3.35 to 3.58) and retinal detachment (3.41, 2.71 to 4.25, and 7.96, 7.63 to 8.30), and very high for retinal vein and artery occlusion.

CONCLUSIONS: With the exception of retinal vascular occlusion, elevations of risk of the ophthalmic diseases studied in hypertension were modest. By contrast, there were significant and substantial increases of risk for each eye disease in people with diabetes.

PMID: 22493039 [PubMed - as supplied by publisher]

Mt Sinai J Med. 2012 Mar;79(2):276-94. doi: 10.1002/msj.21303.

Geriatric vision loss due to cataracts, macular degeneration, and glaucoma.

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Abstract

The major causes of impaired vision in the elderly population of the United States are cataracts, macular degeneration, and open-angle glaucoma. Cataracts and macular degeneration usually reduce central vision, especially reading and near activities, whereas chronic glaucoma characteristically attacks peripheral vision in a silent way, impacting balance, walking, and driving. Untreated, these visual problems lead to issues with regard to taking medications, keeping track of finances and personal information, walking, watching television, and attending the theater, and often create social isolation. Thus, visually

impaired individuals enter nursing homes 3 years earlier, have twice the risk of falling, and have 4× the risk of hip fracture. Consequently, many elderly with low vision exercise greater demands on community services. With the prospect of little improvement and sustained visual loss, in the face of poor tolerance of low-vision services and not accepting magnification as the only way to read, clinical depression is common. In many instances, however, early and accurate diagnosis can result in timely treatment and can preserve quality of life. This review will look at current diagnostic and therapeutic considerations. Currently, about 20.5 million people in the United States have cataracts. The number will reach 30 million by 2020. About 1.75 million Americans currently have some form of macular degeneration, and the number is estimated to increase to 2.95 million in 2020. Approximately 2.2 million Americans have glaucoma, and by 2020 that number is estimated to be close to 3.4 million people. It is projected that by 2030 there will be 72.1 million seniors. With some overlap of the above 3 groups conservatively estimated (if you add the 2030 cataract group to the macular degeneration and glaucoma groups), then about 1 in 2 senior individuals by 2030 may have some significant ocular disease, which could account for about 50% of the healthcare budget for the elderly. Mt Sinai J Med 79:276-294, 2012. © 2012 Mount Sinai School of Medicine.

PMID: 22499498 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2012 Apr 6. [Epub ahead of print]

Association of Vision Loss in Glaucoma and Age-related Macular Degeneration with IADL Disability.

Hochberg C, Maul E, Chan ES, Van Landingham S, Ferrucci L, Friedman DS, Ramulu PY.

Wilmer Eye Institute, Johns Hopkins University, Baltimore, MD, 21287, United States.

Purpose: To determine if glaucoma and/or age-related macular degeneration (AMD) are associated with disability in instrumental activities of daily living (IADLs).

Methods: Glaucoma subjects (n=84) with bilateral visual field (VF) loss and AMD subjects (n=47) with bilateral, or severe unilateral visual acuity (VA) loss were compared to 60 subjects with normal vision (controls). Subjects completed a standard IADL disability questionnaire, with disability defined as an inability to perform 1 or more IADLs unassisted.

Results: Disability in one or more IADLs was present in 18.3% of controls as compared to 25.0% of glaucoma subjects (p=0.34) and 44.7% of AMD subjects (p=0.003). The specific IADL disabilities occurring more frequently in both AMD and glaucoma subjects were: preparing meals, grocery shopping and out-of-home travelling (p<0.05 for both). In multivariate logistic regression models run adjusting for age, gender, mental status, comorbidity and years of education, AMD (OR=3.4, p=0.02) but not glaucoma (OR=1.4, p=0.45) was associated with IADL disability. However, amongst glaucoma and control patients, the odds of IADL disability increased 1.6-fold with every 5 decibels (dB) of VF loss in the better-seeing eye (p=0.001). Additionally, severe glaucoma subjects (better-eye MD worse than -13.5 dB) had higher odds of IADL disability (OR=4.2, p=0.02). Amongst AMD and control subjects, every ETDRS line of worse acuity was associated with a greater likelihood of IADL disability (OR=1.3).

Conclusion: VA loss in AMD and severe VF loss in glaucoma are associated with self-reported difficulties with IADLs. These limitations become more likely with increasing magnitude of VA or VF loss.

PMID: 22491415 [PubMed - as supplied by publisher]

Eye (Lond). 2012 Apr 13. doi: 10.1038/eye.2012.61. [Epub ahead of print]

Visual impairment certification secondary to ARMD in Leeds, 2005-2010: is the incidence falling?

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Aim: The aim of this study was to evaluate trends in visual impairment certification due to age-related macular degeneration (ARMD) in the Leeds metropolitan area between 2005 and 2010.

Methods: In this retrospective study, the primary causes of visual impairment certification in the Leeds metropolitan area between 2005 and 2010 were reviewed. ARMD was considered to be the cause of certification when recorded as the primary factor contributing to visual impairment in one or both eyes. The incidence of visual impairment certification due to ARMD was calculated using population estimates from the Office of National Statistics.

Results: ARMD was the primary cause of visual impairment certification in all study years, accounting for 58.7 and 50.8% of certifications in 2005 and 2010, respectively. For the same period, the incidence of certification due to ARMD fell from 364 to 248 per million population per year. This was largely the result of a fall in the incidence of visual impairment certification due to neovascular ARMD from 225 to 137 per million population per year, beginning in 2008 after the introduction of a local commissioning policy on the use of intra-vitreal ranibizumab.

Conclusion: The incidence of visual impairment certification due to ARMD in the Leeds metropolitan area appears to be falling. This is largely the result of a decrease in certification secondary to neovascular ARMD. This represents a change in the previously described trend for ARMD visual impairment certification.

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Genetics

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ASSOCIATION OF GLUTATHIONE S-TRANSFERASE PI ISOFORM SINGLE-NUCLEOTIDE POLYMORPHISMS WITH EXUDATIVE AGE-RELATED MACULAR DEGENERATION IN A CHINESE POPULATION.

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PURPOSE: To investigate the association between single-nucleotide polymorphisms in the pi isoform of glutathione S-transferase (GSTP1) gene and the risk of exudative age-related macular degeneration (AMD) in a Chinese case-control cohort.

METHODS: A total of 131 Chinese patients with exudative AMD and 138 control individuals were recruited. Genomic DNA was extracted from venous blood leukocytes. Two common nonsynonymous single-nucleotide polymorphisms in GSTP1 (rs1695 and rs4986948) were genotyped by polymerase chain reaction followed by allele-specific restriction enzyme digestion and direct sequencing.

RESULTS: Significant association with exudative AMD was detected for single-nucleotide polymorphism, rs1695 (P = 0.019). The risk G allele frequencies were 21.8% in AMD patients and 12.7% in control subjects (P = 0.007). Compared with the wild-type AA genotype, odds ratio for the risk of AMD was 1.91 (95% confidence interval, 1.09-3.35) for the heterozygous AG genotype and 2.52 (95% confidence interval,

0.6-10.61) for the homozygous GG genotype. In contrast, rs4986948 was not associated with exudative AMD (P = 1.00). The risk G allele frequencies of rs4986948 were 0.4% in AMD patients and 0.4% in control subjects (P = 1.00).

CONCLUSION: Our data suggest that the GSTP1 variant rs1695 moderately increases the risk of exudative AMD. The variant rs4986948 was rare and was not associated with exudative AMD in this Chinese cohort.

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GENOTYPE-PHENOTYPE ASSOCIATIONS IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

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PURPOSE: To examine associations between recognized genetic susceptibility loci and angiographic subphenotypes of the neovascular variant of age-related macular degeneration (nvAMD).

METHODS: Participants (247 nvAMD, 52 early age-related macular degeneration [AMD], and 103 controls) were genotyped (complement factor H and ARMS2/HTRA1). nvAMD participants were assigned to one of two subcategories: mainly classic or mainly occult (based on the proportions of classic and occult choroidal neovascularization). nvAMD and early AMD were reassigned to two groups based on the extent and severity of drusen (retinal pigment epithelium dysfunction or not). Univariate and multivariate analysis were used to examine for associations between participant characteristics and genetic loci after adjusting for age, smoking status, and history of cardiovascular disease.

RESULTS: Univariate analysis confirmed the known significant associations between AMD stage and age, hypertension, and a history of cardiovascular disease. Those with retinal pigment epithelium dysfunction (F = 5.46; P = 0.02) or a positive smoking history (F = 3.89; P = 0.05) were more likely to have been classified as having mainly an occult rather than a mainly classic lesion. Multivariate analysis showed that significant associations were noted with the number of ARMS2/HTRA1 risk alleles (P < 0.001), smoking (ever vs. never) (P = 0.03), and cardiovascular disease (P = 0.01). With early AMD as the reference category, the mainly classic group exhibited significant associations with the number of ARMS2/HTRA1 risk alleles present (P < 0.001) and cardiovascular disease (P = 0.02). When mainly classic was compared with mainly occult, the latter was associated with the ARMS2/HTRA1 locus (P = 0.02).

CONCLUSION: ARMS2/HTRA1 risk genotype may play a role in determining neovascular subphenoptye, whereas genetics/demographics, smoking, and systemic health factors contribute to the development of advanced AMD in the presence of early AMD.

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Association of CFH Y402H Polymorphism with Both Forms of Advanced Age-Related Macular Degeneration in Turkish Patients.

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Purpose: The purpose of this study was to investigate the association between complement factor H Y402H polymorphism and age-related macular degeneration (AMD) development in a cohort of Turkish patients.

Methods: A total of 182 individuals, including 95 individuals with unrelated late age-related macular degeneration and 87 age-matched healthy individuals as a control group were genotyped with polymerase chain reaction followed by restriction enzyme digestion and direct sequence analysis. The statistical analysis was performed with statistical software R 2.9.2 and epicalc package.

Results: The Y402H variant in the CFH gene was found to be associated with late AMD in our study population. Genotypic frequencies were highly different between all patients and control individuals compared for the heterozygotes carrying the risk allele C (AMD patients (CT) 70.5%, control individuals (CT) 54.02%; $\chi(2) = 5.285$, d.f. = 1, p = 0.02). When all AMD patients were compared with the healthy control group, TC heterozygotes showed a significantly increased risk of AMD (O.R = 2.32, CI% 1.23-4.35).

Conclusıon: This study suggests that the CFH Y402H polymorphism is associated with increased risk for both types of end-stage AMD in Turkish patients.

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Clinical Evaluation of 3 Families With Basal Laminar Drusen Caused by Novel Mutations in the Complement Factor H Gene.

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Boon, Smailhodzic, Klevering, den Hollander, and Hoyng and Ms Schoenmaker-Koller) and Human Genetics (Drs Hoefsloot and den Hollander), Radboud University Medical Center, Nijmegen, the Netherlands; Department of Vitreoretinal Surgery, Center for Ophthalmology, University of Cologne, Cologne, Germany (Dr Fauser); and Departments of Ophthalmology and Epidemiology and Biostatistics, Erasmus Medical Center, Rotterdam, the Netherlands (Dr Klaver).

OBJECTIVES: To identify novel complement factor H (CFH) gene mutations and to specify the clinical characteristics in patients with basal laminar drusen (BLD), a clinical subtype of age-related macular degeneration.

METHODS: Twenty-one probands with BLD were included in this study. The ophthalmic examination included nonstereoscopic 30° color fundus photography, fluorescein angiography, and high-resolution spectral-domain optical coherence tomography. Renal function was tested by measurement of serum creatinine and urea nitrogen levels. Venous blood samples were drawn for genomic DNA, and all coding exons and splice junctions of the CFH gene were analyzed by direct sequencing.

RESULTS: In 3 families, we identified novel heterozygous mutations in the CFH gene: p.Ile184fsX, p.Lys204fsX, and c.1697-17_-8del. Ten of 13 mutation carriers displayed the BLD phenotype with a wide variety in clinical presentation, ranging from limited macular drusen to extensive drusen in the posterior pole as well as the peripheral retina. Two patients with BLD developed end-stage kidney disease as a result of membranoproliferative glomerulonephritis type II.

CONCLUSIONS: The early-onset BLD phenotype can be caused by heterozygous mutations in the CFH gene. Because some patients with BLD are at risk to develop membranoproliferative glomerulonephritis type II, we recommend that patients with extensive BLD undergo screening for renal dysfunction. Clinical Relevance Elucidation of the clinical BLD phenotype will facilitate identification of individuals predisposed to developing disease-related comorbidity, such as membranoproliferative glomerulonephritis type II. Moreover, with upcoming treatment modalities targeting specific components of the complement system, early identification of patients with BLD and detection of the genetic defect become increasingly important.

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Differentiation of Exudative Age-related Macular Degeneration and Polypoidal Choroidal Vasculopathy in the ARMS2/HTRA1 Locus.

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Purpose: To differentiate the associations of exudative age-related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV) with the ARMS2/HTRA1 locus.

Methods: The entire ARMS2 sequence was sequenced and HTRA1 rs11200638 genotyped in 568 unrelated Chinese individuals: 156 exudative AMD patients, 164 PCV patients and 248 controls. A meta-analysis was performed to examine the effects of rs10490924 and rs11200638 at the ARMS2/HTRA1 locus in PCV.

Results: In total 31 polymorphisms in ARMS2 were identified. Significant associations with both exudative AMD and PCV were observed in 11 of them and HTRA1 rs11200638, with different genotypic distributions between exudative AMD and PCV ($p < 0.001$). After adjusting for rs11200638, ARMS2 rs10490924 remained significantly associated with exudative AMD ($p = 0.011$), but not with PCV ($p = 0.077$). Meta-analysis showed consistent allelic associations of rs10490924 and rs11200638 with PCV in different study populations.

Conclusion: There is a strong and consistent association of the ARMS2/HTRA1 locus with both exudative AMD and PCV, suggesting the two disorders share, at least partially, similar molecular mechanisms. Different effect sizes indicate the existence of additional genetic and environmental factors affecting them to different extents.

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Zhonghua Yan Ke Za Zhi. 2012 Feb;48(2):176-8.

[Progress in genetic studies of age-related macular degeneration].

[Article in Chinese]

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Abstract

Age related macular degeneration (AMD) is the most common cause of irreversible blindness in the aged population in the western world. AMD is considered to be a multifactorial disease with involvement of both genetic and environmental factors. With the development of molecular biology and molecular genetics, numerous susceptibility genes have been identified. Here we review the recent advances in the genetic studies regarding the AMD susceptibility genes.

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Zhonghua Yan Ke Za Zhi. 2012 Feb;48(2):114-8.

[Use of buccal swab as a source of genomic DNA for genetic screening in patients with age-related macular degeneration].

[Article in Chinese]

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OBJECTIVE: The collection of buccal cells with swabs provides a noninvasive method for obtaining genomic DNA for genetic screening. We aimed to study the feasibility of using buccal swabs for genetic screening in patients with exudative age-related macular degeneration (AMD).

METHODS: Blood and buccal swabs were collected for genetic analysis from 65 patients with exudative AMD. Genomic DNA was isolated from either blood or buccal swabs. The yield of genomic DNA from both sources was determined by spectrophotometer. Genotyping for CFH, LOC387715, and HTRA1 Polymorphisms was performed using a method of polymerase chain reaction (PCR) followed by restriction enzyme digestion. Results using genomic DNA from blood or buccal swabs were compared.

RESULTS: Three swabs were obtained from each patient, 2 from each side of buccal mucosa, and 1 from both upper and inferior gingival mucosa. From swabs with genomic DNA extracted within a week after sample collection, an average of (3.17 ± 1.46) μg genomic DNA was obtained from swab collected from the left or right side buccal mucosa, and (3.94 ± 1.04) μg from swab collected from the upper and inferior gingival mucosa, with relatively higher yield of genomic DNA from the upper and inferior gingival mucosa ($t = 6.79$, $P < 0.05$). From swabs of the left or right side buccal mucosa after being stored at -20°C for 12 months, an average of (3.10 ± 1.17) μg genomic DNA was obtained, which showed no statistically significant difference as compared to the yield of genomic DNA extracted from newly collected swabs ($t = 0.59$, $P > 0.05$). In all 65 patients, genomic DNA isolated from either buccal swabs or blood samples showed exactly the same results regarding the genotypes of CFH, LOC387715, and HTRA1 Polymorphisms.

CONCLUSIONS: Buccal swab is a simple, noninvasive, and reliable source for obtaining genomic DNA. Swabs stored for 12 months at -20°C provide similar amount of genomic DNA as the freshly collected swabs.

PMID: 22490945 [PubMed - in process]

Diet

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Characteristics of patients with wet age-related macular degeneration and low intake of lutein and zeaxanthin.

[Article in English, Spanish]

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OBJECTIVE: To assess the characteristics of patients with wet AMD and low intake of lutein and zeaxanthin in our population.

METHODS: A prospective, observational, cross-sectional study was conducted on patients with active wet

AMD. A full blood count, a lipid and liver profile, a dietary interview (24-hour recall), and an anthropometric study were performed. Lutein-zeaxanthin (LZ) intake results split the patents in two groups.Group 1 ("sufficient" intake): patients with ≥1,400mg/day intake in women and 1,700mg/day in men (2/3 of the average daily intake in a normal population).Group 2: patients with daily intakes below that of group 1. A descriptive and comparative statistical study was performed.

RESULTS: Fifty-two patients with a mean age of 78.9 years. Group 1: eleven patients (21% of the sample). Group 2: forty-one patients. The subjects with adequate intake of LZ had higher a body mass index and waist circumference. Between 70-80% of patients in group 1 had inadequate intake of vitamin A, C and E and zinc.

CONCLUSIONS: Seventy-nine per cent of the patients with wet AMD have a deficient daily intake in lutein-zeaxanthin. The population with adequate intake is associated with an increased body mass index and waist circumference, and in addition, most of them have an insufficient intake of vitamin A, C, E and zinc.

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