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MD Research News

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Drug treatment

Ophthalmologica. 2011 May 5;226(2):45-50. [Epub ahead of print]

Quadruple Therapy Leads to a Sustained Improvement of Vision in Patients with Wet Age-Related Macular Degeneration.

Koss MJ, Lewicka-Chomont A, Schramm K, Rejdak R, Ohrloff C, Koch FH.

Department of Ophthalmology, Johann Wolfgang Goethe University, Frankfurt/Main, Germany.

Abstract

Aim: To investigate the efficacy of a combined intravitreal therapy with prior photodynamic therapy (PDT) in patients with wet age-related macular degeneration. Methods: Fifty-two patients (mean age: 72.7 years) with predominantly classic choroidal neovascularization received low-fluence PDT (42 J/cm(2) for 72 s), followed 24 h later by a 0.4-ml core pars plana vitrectomy with intravitreal injection of dexamethasone (0.8 mg) and bevacizumab (1.25 mg). The best-corrected visual acuity (BCVA; 6 m Snellen), central macular thickness (optical coherence tomography), intraocular pressure and the need for retreatment were assessed. Results: BCVA changed significantly (vs. baseline) at 3 months (+0.11), 9 months (+0.19) and 14 months (+0.16). At the end of the follow-up period, BCVA had improved by >0.1 in the majority of the patients (72.9%), and the mean central retinal thickness had decreased by -44.3% (-211 μm). The retreatment rate was 25%. No increase in intraocular pressure or other adverse event was reported. Conclusions: The pharmacological effects of the drugs, the low-fluence PDT, and the physiological effects of the therapy may have contributed to the sustainability of the therapeutic benefits.

PMID:21546780[PubMed - as supplied by publisher]

Curr Mol Pharmacol. 2011 May 6. [Epub ahead of print]

Dry Age-related Macular Degeneration: Recent Progress of Therapeutic Approaches.

Kuno N, Fujii S.

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Abstract

Age-related macular degeneration (AMD) is a progressive retinal degenerative disease and a common

cause of blindness. In AMD, there are two phenotypes; "atrophic (dry)" and "neovascular (wet)". The former is characterized by the geographic atrophy due to death of retinal pigment epithelium, and the latter is developed due to choroidal neovascularization. While wet AMD can be treated by the inhibition of vascular endothelial growth factor or photodynamic therapy, so far there are no available treatments for dry AMD. Fortunately, understanding of pathogenesis in dry AMD has significantly been progressed and many candidates for the treatment of dry AMD have been introduced in clinical trials as well as preclinical stages. In this article, the progress of therapeutic approaches for dry AMD is reviewed.

PMID:21545354[PubMed - as supplied by publisher]

Ophthalmology. 2011 May;118(5):1004-1004.e1.

Ranibizumab for retinal neovascularization.

Jorge R, Oliveira RS, Messias A, Almeida FP, Strambe ML, Costa RA, Scott IU.

Ribeirão Preto, Brazil.

PMID:21539985 [PubMed - in process]

Publication Types: Letter

Other treatment & diagnosis

Retina. 2011 Apr 27. [Epub ahead of print]

SCANNING LASER OPHTHALMOSCOPE IMAGING STABILIZED MICROPERIMETRY IN DRY AGE-RELATED MACULAR DEGENERATION.

Hartmann KI, Bartsch DU, Cheng L, Kim JS, Gomez ML, Klein H, Freeman WR.

From the *Jacobs Retina Center, Department of Ophthalmology, University of California, San Diego, La Jolla, California; and †Department of Ophthalmology, Ludwig-Maximilians-University Munich, Munich, Germany.

PURPOSE: To determine the effect of drusen and geographic atrophy (GA) in dry age-related macular degeneration on retinal sensitivity using an eye tracking scanning laser ophthalmoscope microperimetry.

METHODS: A total of 44 eyes from 22 patients with dry age-related macular degeneration and drusen and 11 patients with GA were imaged with scanning laser ophthalmoscope microperimetry (OPKO Health, Miami, FL). A custom microperimetry pattern was used to evaluate retinal sensitivity to a Goldmann III size target (108 μm on the retina). The perimetry used a 4-2 stepladder algorithm to determine maximal sensitivity. Microperimetry and optical coherence tomography were performed using a standardized protocol. Twenty-eight eyes with drusen and 16 eyes with GA were analyzed.

RESULTS: Retinal sensitivity overlying drusen was significantly reduced compared with the adjacent uninvolved retina. There was a significant correlation between retinal sensitivity and drusen volume, as well as the grading of the photoreceptor inner segment/outer segment junction score. In patients with GA, an absolute scotoma was confirmed. Retinal sensitivity at the margin of GA was significantly decreased compared with the adjacent uninvolved retina.

CONCLUSION: Scanning laser ophthalmoscope microperimetry is able to detect changes in retinal sensitivity in AMD patients overlying drusen and at the margin of GA. It is a useful device to grade focal retinal sensitivity in patients with dry age-related macular degeneration.

PMID:21540764[PubMed - as supplied by publisher]

Optom Vis Sci. 2011 Apr 28. [Epub ahead of print]

Update on Geographic Atrophy in Age-Related Macular Degeneration.

Biarnés M, Monés J, Alonso J, Arias L.

*OD, MPH †MD ‡MD, PhD Institut de la màcula i la retina, Centre Mèdic Teknon, Barcelona, Spain (MB, JM), Departament de Ciències Experimentals i de la Salut, Universitat Pompeu Fabra, Barcelona, Spain (JA), and Hospital de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain (LA).

Abstract

Age-related macular degeneration (AMD) is the main cause of legal blindness in older patients in developed countries, and geographic atrophy (GA) represents the advanced form of dry AMD. Although it accounts for one third of the cases of late AMD and is responsible for 20% of the cases of severe visual loss due to the disorder. GA currently lacks effective treatment, whereas antiangiogenic therapies have been shown to be successful in managing choroidal neovascularization, the other form of late AMD. Recent advances in GA epidemiology, etiology, genetics, and imaging techniques have renewed the interest in this entity, which is a cause of progressive visual loss even in treated patients with neovascular AMD. This knowledge has triggered many clinical trials targeting different molecules shown to be associated with the disease, and it is hoped that this research will translate into effective drugs for GA in the near future.

PMID:21532519[PubMed - as supplied by publisher]

J Am Acad Dermatol. 2011 Apr 30. [Epub ahead of print]

Ocular hazards of blue-light therapy in dermatology.

Walker DP, Vollmer-Snarr HR, Eberting CL.

University of Texas Southwestern Medical Center, Dallas, Texas.

Abstract

Blue-light phototherapy has become important in the treatment of many dermatologic conditions and as a result continue to be developed. Although blue-light therapy is successful, research shows that excessive ocular blue-light exposure may contribute to age-related macular degeneration and other vision problems. As blue-light therapy becomes increasingly more popular for clinical and at-home use, patients and operators of blue-light devices should be aware of its associated ocular hazards. Protective eyewear should be carefully selected and implemented with each therapy session to guard against the development of retinal disease.

PMID:21536341[PubMed - as supplied by publisher]

Epidemiology & pathogenesis

Jpn J Ophthalmol. 2011 May 3. [Epub ahead of print]

Characteristics of age-related macular degeneration in patients with diabetic retinopathy.

Yoshikawa T, Ogata N, Wada M, Otsuji T, Takahashi K.

Department of Ophthalmology, Kansai Medical University, Takii Hospital, Osaka, Japan.

PURPOSE: The purpose of this study was to determine the clinical characteristics of age-related macular degeneration (AMD) in patients with diabetic retinopathy (DR).

METHODS: Retrospective, consecutive case series. Twenty-six eyes of 25 Japanese patients were studied. All patients were diagnosed as having exudative AMD with DR. Patients with no apparent DR, dry AMD, neovascular maculopathy associated with high myopia, and age <50 years were excluded. The clinical characteristics of AMD in patients with DR, e.g., gender, age, stage of DR, and type of AMD were evaluated.

RESULTS: In the 26 eyes, 2 eyes (7.7%) were classified as mild nonproliferative DR (NPDR), 7 (27.0%) with moderate NPDR, 16 (61.5%) with severe NPDR and 1 eye (3.8%) with PDR. Of the 26 eyes with exudative AMD, 21 eyes (80.8%) were classified as neovascular AMD, 4 (15.4%) as polypoidal choroidal vasculopathy and 1 eye (3.8%) as a retinal angiomatous proliferation. Among the eyes with neovascular AMD, 9 eyes (42.9%) were classified as predominantly classic choroidal neovascularization (CNV).

CONCLUSIONS: There is a predominance of men, neovascular AMD and predominantly classic CNV in Japanese AMD patients with DR. The exudative AMD in patients with DR may have different clinical characteristics from those without DR.

PMID:21538005 [PubMed - as supplied by publisher]

World J Biol Chem. 2010 Dec 26;1(12):369-76.

Suofu Qin's work on studies of cell survival signaling in cancer and epithelial cells.

Qin S.

Suofu Qin, Retinal Disease Research, Department of Biological Sciences, Allergan, Inc., 2525 Dupont Drive, Irvine, CA 92612-1599, United States.

Abstract

Reactive oxygen species (ROS) encompass a variety of diverse chemical species including superoxide anions, hydrogen peroxide, hydroxyl radicals and peroxynitrite, which are mainly produced via mitochondrial oxidative metabolism, enzymatic reactions, and light-initiated lipid peroxidation. Over-production of ROS and/or decrease in the antioxidant capacity cause cells to undergo oxidative stress that damages cellular macromolecules such as proteins, lipids, and DNA. Oxidative stress is associated with ageing and the development of age-related diseases such as cancer and age-related macular degeneration. ROS activate signaling pathways that promote cell survival or lead to cell death, depending on the source and site of ROS production, the specific ROS generated, the concentration and kinetics of ROS generation, and the cell types being challenged. However, how the nature and compartmentalization of ROS contribute to the pathogenesis of individual diseases is poorly understood. Consequently, it is crucial to gain a comprehensive understanding of the molecular bases of cell oxidative stress signaling, which will then provide novel therapeutic opportunities to interfere with disease progression via targeting specific signaling pathways. Currently, Dr. Qin's work is focused on inflammatory and oxidative stress responses using the retinal pigment epithelial (RPE) cells as a model. The study of RPE cell inflammatory and oxidative stress responses has successfully led to a better understanding of RPE cell biology and identification of potential therapeutic targets.

PMID:21537472[PubMed - in process] PMCID: PMC3083942

Proc Natl Acad Sci U S A. 2011 May 2. [Epub ahead of print]

Regulation of angiogenesis and choroidal neovascularization by members of microRNA-23~27~24 clusters.

Zhou Q, Gallagher R, Ufret-Vincenty R, Li X, Olson EN, Wang S.

Departments of Ophthalmology, Molecular Biology, and Pharmacology, University of Texas Southwestern Medical Center, Dallas, TX 75390.

Abstract

MicroRNAs (miRNAs) modulate complex physiological and pathological processes by repressing expression of multiple components of cellular regulatory networks. Here we demonstrate that miRNAs encoded by the miR-23~27~24 gene clusters are enriched in endothelial cells and highly vascularized tissues. Inhibition of miR-23 and miR-27 function by locked nucleic acid-modified anti-miRNAs represses angiogenesis in vitro and postnatal retinal vascular development in vivo. Moreover, miR-23 and miR-27 are required for pathological angiogenesis in a laser-induced choroidal neovascularization mouse model. MiR-23 and miR-27 enhance angiogenesis by promoting angiogenic signaling through targeting Sprouty2 and Sema6A proteins, which exert antiangiogenic activity. Manipulating miR-23/27 levels may have important therapeutic implications in neovascular age-related macular degeneration and other vascular disorders.

PMID:21536891[PubMed - as supplied by publisher]

Br J Ophthalmol. 2011 May 5. [Epub ahead of print]

Cytokines in neovascular age-related macular degeneration: fundamentals of targeted combination therapy.

Dias JR, Rodrigues EB, Maia M, Magalhães O Jr, Penha FM, Farah ME.

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Abstract

The neovascular form of age-related macular degeneration (AMD), called wet-AMD or choroidal neovascularisation, begins with damage to the outer retinal cells and retinal pigment epithelium (RPE), which elicits a cascade of inflammatory and angiogenic responses leading to neovascularisation under the macula. Studies showed that oxidative damage, chronic inflammation of the RPE and complement misregulation work at different steps of this disease. After established neovascularisation, several pro- and antiangiogenic agents start to play an important role. Vascular endothelial growth factors (VEGFs) are the most specific and potent regulators of angiogenesis, which are inhibited by intravitreal injections of ranibizumab, bevacizumab, VEGF Trap, pegaptanib sodium and other agents under investigation. Pigment epithelium-derived factor, on the other hand, shows neuroprotective and antiangiogenic activities. Hepatocyte growth factor (HGF) has a mitogenic effect on a wide range of epithelial and endothelial cells, and it is inhibited by an anti-HGF monoclonal antibody. Platelet-derived growth factor is a potent chemoattractant and mitogen for both fibroblasts and retinal RPE cells, which has been inhibited experimentally by VEGF Trap and human anti-platelet-derived growth factor-D monoclonal antibody. Fibroblast growth factor-2 has pleiotropic effects in different cell and organ systems, and it is blocked by anti-FGF antibodies, with a greater benefit regarding antiangiogenesis when combined treatment with anti-VEGF is performed. Tumour necrosis factor alpha is expressed in the retina and the choroid, and its blockade in choroidal neovascularisation includes the use of monoclonals such as infliximab. This paper reviews the most important cytokines involved in the pathogenesis of wet-AMD, with emphasis on potential combined therapies for disease control.

PMID:21546514[PubMed - as supplied by publisher]

BMC Ophthalmol. 2011 May 5;11(1):10. [Epub ahead of print]

Causes and 3-year-incidence of blindness in Jing-An District, Shanghai, China 2001-2009.

Wu L, Sun X, Zhou X, Weng C.

BACKGROUND: Registered data can provide valuable information regarding blindness. The purpose of this study was to evaluate the main causes and 3-year incidence of registered blindness in Jing-An district in Shanghai, China.

METHODS: Data from the blindness registry (age, gender and cause of visual disability) were collected and analyzed. The prevalence of blindness for 2003, 2007, 2009 and the 3-year incidence of blindness were calculated.

RESULTS: The prevalence increased significantly from 113.7 per 100,000 in 2003 to 145.8 per 100,000 in 2006 to 165.9 per 100,000 in 2009 (P<0.05, P<0.05, respectively). Age can significantly affect prevalence; the odd ratios (OR) were 2.57 in the 30 y - 49 y range (P<0.001), 7.27 in the 50 y - 69 y range (P<0.001) and 21.2 in the >70 y (P<0.001). The 3-year incidence increased from 32.3 per 100,000 in 2001-2003 to 34.2 per 100,000 in 2004-2006 to 40.8 per 100,000 in 2007-2009. The causes of new blindness registered in 2001-2009 were myopic macular degeneration (19.40%), followed by glaucoma (17.67%), age-related macular degeneration (11.78%), optical nerve atrophy (9.43%), retinitis pigmentosa (8.62%), diabetic retinopathy (7.76%) and corneal opacity (5.75%).

CONCLUSIONS: The 3-year incidence and prevalence of registered blindness increased in the past 9 years. The leading causes of new blindness were myopic macular degeneration, glaucoma and age-related macular degeneration. The pattern of causes has changed little in the past 9 years and is different from other locations in China. The pattern is similar to that of Taiwan, Hongkong, and Western countries.

PMID:21545726[PubMed - as supplied by publisher]

Genetics

Mol Vis. 2011 Apr 20;17:997-1002.

Apolipoprotein E gene and age-related macular degeneration in a Chinese population.

Sun E, Lim A, Liu X, Snellingen T, Wang N, Liu N.

PURPOSE: To examine the association between apolipoprotein E (APOE) polymorphisms and age-related macular degeneration (AMD) in a Chinese population.

METHODS: The study consisted of 712 subjects, including 201 controls, 363 cases with early AMD, and 148 cases with exudative AMD. Genomic DNA was extracted from venous blood leukocytes. Common allelic variants of APOE (e2, e3, and e4) were analyzed by PCR and direct sequencing.

RESULTS: APOE e3e3 was the most frequent genotype, with a frequency of 72.6% in controls, 72.5% in early AMD, and 70.3% in exudative AMD. Frequency of the e2 allele was 6.7% in controls, 7.4% in early AMD, and 8.8% in exudative AMD. Frequency of the e4 allele was 8.7% in controls, 7.7% in early AMD, and 7.8% in exudative AMD. No statistically significant difference in APOE genotype and allele frequency distribution was observed among controls, cases with early AMD, and cases with exudative AMD. For e2 allele carriers, the odds ratio was 1.12 (95% confidence interval [CI], 0.65-1.93) for early AMD and 1.06 (95% CI, 0.53-2.10) for exudative AMD. For e4 allele carriers, the odds ratio was 1.04 (95% CI, 0.61-1.75) for early AMD and 0.83 (95% CI, 0.42-1.62) for exudative AMD.

CONCLUSIONS: Our data provide no evidence to support an association of APOE polymorphisms with early or exudative AMD, suggesting that APOE is less likely to be a major AMD susceptibility gene in the Chinese population.

PMID:21541275[PubMed - in process] PMCID: PMC3084239

Mol Vis. 2011 Apr 20;17:977-82.

The association of age-related maculopathy susceptibility 2 polymorphisms with phenotype in typical neovascular age-related macular degeneration and polypoidal choroidal vasculopathy.

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Department of Surgery, Division of Ophthalmology, Kobe University Graduate School of Medicine, Kobe, Japan.

PURPOSE: To determine the association of age-related maculopathy susceptibility 2 (ARMS2) gene polymorphisms with the phenotype of typical neovascular age-related macular degeneration (tAMD) and polypoidal choroidal vasculopathy (PCV) and the effects of photodynamic therapy (PDT).

METHODS: The single nucleotide polymorphisms at rs10490924 (A69S) in ARMS2 of 68 tAMD and 119 PCV patients who underwent PDT were genotyped using the TaqMan assay. The baseline best corrected visual acuity (BCVA) and lesion size were compared among the three genotypes at rs10490924. A multivariate regression analysis was performed to evaluate the influence of the baseline BCVA, greatest linear dimension (GLD), and lesion phenotype (tAMD or PCV) on the association of rs10490924 with the BCVA 12 months after the first PDT.

RESULTS: The mean lesion size was significantly different among the GG, GT, and TT genotypes at rs10490924 in the PCV group, although no significant differences were detected in the tAMD group. PCV patients with a G allele had significantly better vision at 3 months after the initial PDT. tAMD patients with a TT genotype had significantly poorer vision at 12 months after the first PDT. In the multivariate regression analysis, the additive model of the G allele at rs10490924 was associated with a significantly better BCVA 12 months after the first PDT in tAMD and PCV patients.

CONCLUSIONS: ARMS2 variants are likely associated with the phenotype and the effects of PDT in tAMD and PCV.

PMID:21541271[PubMed - in process] PMCID: PMC3084225

Mol Vis. 2011 Apr 20;17:983-8.

Complement factor B polymorphism 32W protects against age-related macular degeneration.

Hughes AE, Mullan GM, Bradley DT.

Centre for Public Health, Queen's University Belfast, UK.

PURPOSE: The 32Q (rs641153; A) and 32W (rs12614; T) variants of complement factor B (CFB) cause less efficient complement activation in vitro than the common 32R variant. This is thought to be the reason that the 32Q variant is associated with decreased risk of age-related macular degeneration (AMD). We investigated whether the 32W variant was also associated with decreased risk of AMD.

METHODS: We genotyped 367 cases with neovascular AMD and 251 disease-free controls. Association with the disease phenotype was assessed by logistic regression for polymorphisms of CFB alone and in combination with smoking status and genetic risk markers of complement factor H (CFH) and HtrA serine peptidase 1 (HTRA1). We performed meta-analysis of all previously published reports of 32W allele frequency in AMD cases and controls.

RESULTS: The CFB variant 32W was associated with protection against neovascular AMD, compared to the common 32R variant (odds ratio 0.64, $p<0.05$, in logistic regression with CFB variants; odds ratio 0.53, $p<0.05$, in logistic regression with CFB variants, CFH haplotypes, HTRA1 rs10490924 genotype, and smoking status). Meta-analysis (n=1,795) including this study and two others of neovascular AMD showed a combined odds ratio of 0.75 ($p<0.05$) for 32W, compared to 32R. Meta-analysis (n=2,600) of all reported

studies of all types of AMD showed a combined odds ratio of 0.79 ($p<0.01$).

CONCLUSIONS: Our study shows that the 32W variant of CFB is associated with protection against AMD, in keeping with evidence of its functional effect on the complement system. The protective effect is less strong than that associated with 32Q.

PMID:21541267[PubMed - in process] PMCID: PMC3084221