Macular Degeneration Foundation
Our focus is your vision

MD Research News

Issue 78

Monday April 30, 2012

This free weekly bulletin lists the latest published research articles on macular degeneration (MD) as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term “macular degeneration”.

If you have not already subscribed, please email Rob Cummins at **research@mdfoundation.com.au** with ‘Subscribe to MD Research News’ in the subject line, and your name and address in the body of the email.

You may unsubscribe at any time by an email to the above address with your ‘unsubscribe’ request.

Drug treatment

Br J Ophthalmol. 2012 Apr 26. [Epub ahead of print]

Actions of bevacizumab and ranibizumab on microvascular retinal endothelial cells: similarities and differences.

Deissler HL, Deissler H, Lang GE.

University of Ulm, Ulm, Germany.

BACKGROUND: Retinal endothelial cells are crucially involved in the genesis of diabetic retinopathy which is treated with vascular endothelial growth factor (VEGF) inhibitors. Of these, ranibizumab can completely restore VEGF-induced effects on immortalised bovine retinal endothelial cells (iBREC). In most experiments supporting diabetic retinopathy therapy with bevacizumab, only non-retinal EC or retinal pigment epithelial cells have been used. Also, bevacizumab but not ranibizumab can accumulate in retinal pigment epithelial cells.

OBJECTIVE: To investigate the effects of bevacizumab on VEGF-induced changes of iBREC properties and potential uptake and accumulation of both inhibitors.

METHODS: Uptake of VEGF inhibitors by iBREC with or without pretreatment with VEGF(165) was visualised by immunofluorescence staining and western blot analyses. Measured transendothelial resistance (TER) of iBREC (±VEGF(165)) showed effects on permeability, indicated also by the western blot-determined tight junction protein claudin-1. The influence of bevacizumab on proliferation and migration of iBREC was studied in the presence and absence of VEGF(165).

RESULTS: Bevacizumab strongly inhibited VEGF-stimulated and basal migration, but was less efficient than ranibizumab in inhibiting VEGF-induced proliferation or restoring the VEGF-induced decrease of TER and claudin-1. This ability was completely lost after storage of bevacizumab for 4 weeks at 4°C. Ranibizumab and bevacizumab were detectable in whole cell extracts after treatment for at least 1 h; bevacizumab accumulated during prolonged treatment. Ranibizumab was found in the membrane/organelle fraction, whereas bevacizumab was associated with the cytoskeleton.

CONCLUSION: Both inhibitors had similar effects on retinal endothelial cells; however, some differences were recognised. Although barrier properties were not affected by internalised bevacizumab in vitro, potential adverse effects due to accumulation after repetitive intravitreal injections remain to be investigated.

PMID: 22539748 [PubMed - as supplied by publisher]

Retina. 2012 May;32(5):949-55.

Prognostic factors for visual outcome after intravitreal anti-VEGF injection for naive myopic choroidal neovascularization.

Yoon JU, Kim YM, Lee SJ, Byun YJ, 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 School of Medicine, Gyeonggido, Korea.

PURPOSE: The aim of this study was to evaluate the prognostic factors of visual outcome after intravitreal anti-vascular endothelial growth factor injection in patients with myopic choroidal neovascularization (CNV).

METHODS: Forty eyes of 40 consecutive patients with myopic CNV who had received intravitreal ranibizumab or bevacizumab injections were retrospectively reviewed. Baseline visual acuity, presence of lacquer crack, dark rim, peripapillary choroidal atrophy size, and location of myopic CNV were evaluated using fluorescein angiography and indocyanine green angiography.

RESULTS: The logarithm of the minimum angle of resolution best-corrected visual acuity (BCVA) at 12 months after treatment was 0.23 ± 0.28, and there was a significant improvement compared with the baseline BCVA (P = 0.001). After multiple linear regression analysis, baseline BCVA, presence of lacquer crack extending the fovea, and peripapillary choroidal atrophy size were the factors that significantly correlated with BCVA at 12 months (P = 0.001, P = 0.04, and P = 0.04). For mean change in BCVA over 12 months, there were also significant correlations with baseline BCVA, lacquer crack extension to the fovea, and peripapillary choroidal atrophy size (P = 0.001, P = 0.03, and P = 0.03). The mean number of anti-vascular endothelial growth factor injections was 2.8 ± 2.0 over 12 months. Complete resolution of myopic CNV was noted in 22 eyes (55.0%) after initial first injection, and no additional treatment was required in 12 eyes (30%).

CONCLUSION: Better baseline BCVA, lacquer crack extension to the fovea, and peripapillary atrophy were negative prognostic factors of visual acuity improvement, and there was quite a promising result of anti-vascular endothelial growth factor treatment in patients with myopic CNV.

PMID: 22534553 [PubMed - in process]

Case Report Ophthalmol. 2012 Jan;3(1):77-82. Epub 2012 Feb 29.

Intravitreal ranibizumab in the treatment of butterfly-shaped pattern dystrophy associated with choroidal neovascularization: a case report.

Empeslidis T, Vardarinos A, Deane J, Banerjee S.

Leicester Royal Infirmary, University Hospitals of Leicester, Leicester, UK.

PURPOSE: To present and document the effectiveness of intravitreal ranibizumab in the treatment of patients with choroidal neovascularization due to butterfly-shaped pattern dystrophy (PD) of the macula.

METHODS: Three intravitreal ranibizumab injections of 0.5 mg/0.05 ml in monthly intervals were given to a patient with a previously diagnosed butterfly-shaped PD who subsequently developed subfoveal choroidal neovascularization on the right eye. The patient had previously received a combination of verteporfin/ photodynamic therapy for a juxtafoveal choroidal neovascular membrane on the left eye.

RESULTS: At the end of the treatment course, there was significant improvement of the patient's vision and the appearance of the macula on optic coherence tomography and fluorescein angiography. Best-corrected visual acuity improved from 6/12 to 6/6 and retinal thickness at the macula decreased from 323 to 247 μm. No subretinal fluid remained. The patient is clinically stable over a 12-month follow-up period.

CONCLUSIONS: Intravitreal ranibizumab seems to be an effective and safe option for the treatment of subfoveal choroidal neovascularization in patients with butterfly-shaped PD.

PMID: 22529806 [PubMed - in process] PMCID: PMC3331880

Int Ophthalmol. 2012 Apr 18. [Epub ahead of print]

Visual and morphological outcomes of bevacizumab (Avastin(®)) versus ranibizumab (Lucentis (®)) treatment for retinal angiomatous proliferation.

Hufendiek K, Hufendiek K, Panagakis G, Helbig H, Gamulescu MA.

Department of Ophthalmology, University Medical Center Regensburg, Regensburg, Germany, katerina.hufendiek@klinik.uni-regensburg.de.

Abstract

Retinal angiomatous proliferation (RAP) is a variant of exudative age-related macular degeneration with particularly bad prognosis. The purpose of this work is to describe the long-term functional and morphological outcome of patients treated with intravitreal bevacizumab and ranibizumab. Retrospective case series of 16 eyes treated with bevacizumab and 19 eyes treated with ranibizumab. All patients received initially three intravitreal injections of bevacizumab (1.25 mg/0.05 ml) or ranibizumab (0.5 mg/0.05 ml) every 4 weeks. Follow-up ranged from 1 to 7 months after the third injection. Complete ophthalmologic examination including best-corrected visual acuity (VA), optical coherence tomography, fluorescein angiography, and in selected cases, indocyanine green angiography was performed. Triple intravitreal injections resulted in improvement of VA in bevacizumab-treated as well as in ranibizumab-treated patients; logarithm of the minimal angle of resolution (logMAR) 0.84 before treatment and 0.67 at month 9, and logMAR 0.75 before treatment and 0.59 at month 9, respectively. Central macular thickness (CMT) in the bevacizumab group improved from 363.67 ± 47.4 μm at baseline to 328 ± 49.77 μm at month 6 ($p = 0.03$) and 301 ± 129.69 at month 9 ($p = 0.35$). CMT in the ranibizumab group improved from 545.62 ± 167.39 μm at baseline to 395.88 ± 169.37 μm at month 6 and 411.83 ± 212.41 μm at month 9 ($p = 0.03$, $p = 0.05$, respectively). Patients with RAP might benefit from both intravitreal bevacizumab and ranibizumab treatments with stabilization of VA over a longer period of time. Close follow-up should nevertheless be performed in this special subgroup because of the high recurrence rate.

PMID: 22527448 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2012 Apr 25. [Epub ahead of print]

Ranibizumab for serous macular detachment in branch retinal vein occlusions.

Gallego-Pinazo R, Dolz-Marco R, Pardo-López D, Martínez-Castillo S, Lleó-Pérez A, Arévalo JF, Díaz-Llopis M.

Department of Ophthalmology, University and Polytechnic Hospital La Fe, Bulevar Sur s/n, 46026, Valencia, Spain.

BACKGROUND: The purpose of this study was to compare the efficacy of intravitreal ranibizumab in the treatment of macular edema due to branch retinal vein occlusions (BRVO) with and without serous macular neuroretinal detachment (SMD).

METHODS: Forty-nine eyes of 49 patients with macular edema due to branch retinal vein occlusion (22 with SMD and 27 without SMD) were included in this prospective, parallel-group, comparative study. Intravitreal injection of ranibizumab was administered at baseline. Thereafter patients were followed monthly and further injections were performed in the presence of persistence or recurrence of macular

thickening. Flattening of the macula was considered success. At the last visit, best-corrected visual acuity (BCVA), and spectral-domain optical coherence tomography (SD-OCT) quantitative parameters (central subfield thickness, cube volume, average cube thickness) were compared between groups.

RESULTS: In patients with SMD, BCVA and all the SD-OCT quantitative parameters improved significantly after a mean number of 5.0 ranibizumab intravitreal injections through a median follow-up of 12.5 months (range, 7-34). In patients without SMD, all the variables analyzed improved significantly except for the cube volume, after a mean number of 4.3 ranibizumab intravitreal injections through a median follow-up of 10.4 months (range, 6.5-40.2). The numbers of injections were similar in both groups. The final BCVA was better in patients without SMD at baseline but without significant differences in the SD-OCT parameters between groups.

CONCLUSIONS: The presence of SMD may be a baseline predictive factor for ranibizumab treatment outcomes in BRVO patients, with no influence in the number of treatments needed between patients with or without SMD at baseline. Further studies are needed in order to confirm the role of SMD as an independent predicitive factor in cases of BRVO.

PMID: 22527327 [PubMed - as supplied by publisher]

Ophthalmologica. 2012;227 Suppl 1:11-20. Epub 2012 Apr 24.

Neovascular age-related macular degeneration.

Veritti D, Sarao V, Lanzetta P.

Department of Ophthalmology, University of Udine, Udine, Italy.

Purpose: Neovascular age-related macular degeneration (AMD) is a leading cause of blindness, with an increasing incidence as the elderly population expands. Large, multi-center, randomized, clinical trials have been conducted exploring the safety and efficacy of anti-VEGF treatments. This paper aims to discuss the safety and efficacy of pegaptanib, ranibizumab, aflibercept and bevacizumab. New therapeutic agents and treatment strategies are also discussed.

Procedures: Evidence available from prospective, multicenter, clinical studies and from a selective literature search is utilized to present the results of VEGF inhibition in neovascular AMD and to generate evidence-based recommendations.

Results: Anti-VEGF treatment is indicated in choroidal neovascularization with active disease and produces a significant benefit in visual acuity.

Conclusions: With the advent of anti-VEGF therapy, the prognosis of choroidal neovascularization has changed dramatically. Data from well-conducted clinical trials suggest that approved anti-VEGF drugs are effective and well tolerated.

PMID: 22517121 [PubMed - in process]

Graefes Arch Clin Exp Ophthalmol. 2012 Apr 25. [Epub ahead of print]

Ranibizumab is not bevacizumab for retinal vein occlusions.

Gallego-Pinazo R, Dolz-Marco R, Díaz-Llopis M.

Unit of Macula. Department of Ophthalmology, University and Polytechnic Hospital La Fe, Bulevar Sur, s/n, 46026, Valencia, Spain, robertogallego@comv.es.

PMID: 22527322 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2012 Apr 15. [Epub ahead of print]

FUSION regimen: ranibizumab in treatment-naïve patients with exudative age-related macular degeneration and relatively good baseline visual acuity.

Monés J, Biarnés M, Trindade F, Casaroli-Marano R.

Institut de la Màcula i de la Retina, Centro Médico Teknon, Vilana 12, Barcelona, 08022, Spain, jmones@institutmacularetina.com.

BACKGROUND: To investigate the safety and efficacy of a combined fixed-interval and pro re nata regimen of ranibizumab (FUSION regimen) for treatment of exudative age-related macular degeneration in patients with good visual acuity at baseline. To establish whether similar efficacy to monthly regimens can be achieved with fewer injections, even in patients with good visual acuity.

METHODS: This was a prospective, open-label, consecutive interventional case series in treatment-naïve patients with exudative age-related macular degeneration. The FUSION regimen consists of three phases: 1) a loading phase of two or three injections, depending on presence or absence of choroidal neovascularization activity at first follow-up, 2) administration of one injection on disappearance of exudation, and 3) subsequent administration of two separate injections at intervals 2 months apart, and then an injection every 3 months. Endpoints included visual acuity, presence of fluid, adverse events and number of injections administered.

RESULTS: Seventeen eyes of 17 Caucasian patients were included. Mean patient age was 76 years, and 15 patients were female. Mean baseline visual acuity was 67.5 letters (median 67), with Snellen equivalent 20/50++, ranged between 45 (20/125) and 83 (20/20--). At 3 months, mean change in best-corrected visual acuity (BCVA) was +2.3 letters (median +9) compared with baseline ($p = 0.3$). At 6 months, mean change in BCVA was +4.2 letters (median +9) compared with baseline ($p = 0.02$). At 12 months, one patient had discontinued the study. Mean change in BCVA was 5.6 (median +10) compared with baseline ($p = 0.04$). No patient lost ≥15 letters, and 14 patients (87.5%) lost <5 letters. The mean number of injections was 6.9. One patient experienced a retinal pigment epithelium tear; no other complications were observed.

CONCLUSIONS: The FUSION regimen for ranibizumab has the potential to maintain visual gains achieved during the loading phase, as reported in studies with monthly injections, even in eyes with a relatively good visual acuity at baseline. These 12-month results warrant validation in a larger, randomized controlled trial.

PMID: 22527314 [PubMed - as supplied by publisher]

Prog Retin Eye Res. 2012 Apr 11. [Epub ahead of print]

Bacterial endophthalmitis in the age of outpatient intravitreal therapies and cataract surgeries: Host-microbe interactions in intraocular infection.

Sadaka A, Durand ML, Gilmore MS.

Department of Ophthalmology, Harvard Medical School, Boston, MA 02114, USA; Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, USA.

Abstract

Bacterial endophthalmitis is a sight threatening infection of the interior structures of the eye. Incidence in the US has increased in recent years, which appears to be related to procedures being performed on an aging population. The advent of outpatient intravitreal therapy for management of age-related macular degeneration raises yet additional risks. Compounding the problem is the continuing progression of antibiotic resistance. Visual prognosis for endophthalmitis depends on the virulence of the causative organism, the severity of intraocular inflammation, and the timeliness of effective therapy. We review the

current understanding of the pathogenesis of bacterial endophthalmitis, highlighting opportunities for the development of improved therapeutics and preventive strategies.

PMID: 22521570 [PubMed - as supplied by publisher]

J Ophthalmol. 2012;2012:786870. Epub 2012 Feb 28.

Anti-VEGF Treatment Strategies for Wet AMD.

Kovach JL, Schwartz SG, Flynn HW Jr, Scott IU.

Department of Ophthalmology, Bascom Palmer Eye Institute, School of Medicine, University of Miami, 311 9th St North, Naples, FL 34102, USA.

Abstract

Over the past few years, antivascular endothelial growth factor (VEGF) therapy has become a standard treatment for neovascular age-related macular degeneration (AMD). During this time, treatment strategies have evolved from a monthly dosing schedule to individualized regimens. This paper will review the currently available anti-VEGF agents and evidence-based treatment strategies.

PMID: 22523653 [PubMed - in process] PMCID: PMC3317200

Acta Ophthalmol. 2012 Apr 20. doi: 10.1111/j.1755-3768.2012.02433.x. [Epub ahead of print]

A new fractioning process to decrease the price of ranibizumab.

González-Andrades M, Muñoz-Ávila JI, Medarde-Caballero C, Fernández-López C, Damas-Alonso M.

Ophthalmology Service, San Cecilio University Hospital, Granada, Spain Pharmacy Service, San Cecilio University Hospital, Granada, Spain.

PMID: 22520334 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Br J Ophthalmol. 2012 Apr 25. [Epub ahead of print]

Patients' preferences in treatment for neovascular age-related macular degeneration in clinical routine.

Finger R, Hoffmann AE, Fenwick EK, Wolf A, Kampik A, Kernt M, Neubauer AS, Hirneiss C.

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

PURPOSE: To assess the effect of ranibizumab treatment for neovascular age-related macular degeneration (nvAMD) on patients' preferences and vision-related quality of life (VRQoL) in a routine clinical setting.

METHODS: 55 treatment naïve patients were examined before and after the initial upload of three monthly injections of 0.5 mg ranibizumab. VRQoL was assessed using a Rasch-adjusted NEI-VFQ-25. Time trade-off (TTO), standard gamble, a visual analogue scale and the European Quality of Life Questionnaire (EQ-5D) were used to calculate utilities, and multiple logistic regression models were conducted to determine independent factors associated with utilities.

RESULTS: Mean±SD age was 75±7 years, and 40 patients (73%) were female. Mean±SD best-corrected visual acuity of the treated eye increased from 20/80 at baseline (logMAR 0.60±0.35) to 20/63 (logMAR 0.52±0.36; p=0.020) at follow-up after three injections. Utility score increases ranged from 2 utils (standard gamble anchored for death) up to 6.6 utils (EQ-5D German TTO, p=0.023) and visual functioning improved (Rasch adjusted composite NEI-VFQ score 50±21 to 54±21, p=0.042). Whether the worse or better eye was treated was not significantly associated with improvements in utility or VRQoL, whereas VA improvement in the treated eye was associated with an increase in utility (TTO, p=0.020).

CONCLUSIONS: TTO performed best in this sample of elderly nvAMD patients undergoing anti-VEGF therapy. Better or worse eye treatment was not associated with a change in reported utilities or visual functioning in patients with newly diagnosed nvAMD. Directly elicited, vision-specific utilities gained with TTO seem to be sensitive to a change in vision status.

PMID: 22535331 [PubMed - as supplied by publisher]

J Biomed Mater Res A. 2012 Apr 24. doi: 10.1002/jbm.a.34178. [Epub ahead of print]

Developing methacrylate-based copolymers as an artificial Bruch's membrane substitute.

Treharne AJ, Thomson HA, Grossel MC, Lotery AJ.

Faculty of Natural and Environmental Sciences, University of Southampton, Southampton SO17 1BJ, United Kingdom.

Abstract

Age-related macular degeneration (AMD) is the most common cause of blindness in the developed world. There is currently no treatment for the cellular loss, which is characteristic of AMD. Transplantation of retinal pigment epithelium (RPE) cells represents a potential therapy. Because of AMD-related pathology in the native support, Bruch's membrane, transplanted RPE cells require a scaffold to reside on. We present here the development of an electrospun fibrous scaffold derived from methyl methacrylate and poly (ethylene glycol) (PEG) methacrylate for novel application as an RPE scaffold. Scaffolds were chemically modified to improve cell adhesion by functionalization not previously reported for this type of copolymer system. A human RPE cell line was used to investigate cell-scaffold interactions for up to two weeks in vitro. Scanning electron microscopy was used to characterize the fibrous scaffolds and confirm cell attachment. By day 15, cell area was significantly ($p < 0.001$) enhanced on scaffolds with chemical modification of the PEG chain terminus. In addition, significantly, less-apoptotic cell death was demonstrable on these modified surfaces. © 2012 Wiley Periodicals, Inc. J Biomed Mater Res Part A, 2012.

PMID: 22528296 [PubMed - as supplied by publisher]

J Ophthalmol. 2012;2012:851648. Epub 2012 Mar 19.

Predictive Factors in OCT Analysis for Visual Outcome in Exudative AMD.

Gamulescu MA, Panagakis G, Theek C, Helbig H.

University Eye Clinic, Franz-Josef-Strauss Allee 11, 93051 Regensburg, Germany.

Background: Reliable predictive factors for therapy outcome may enable treating physicians to counsel their patients more efficiently concerning probability of improvement or time point of discontinuation of a certain therapy.

Methods: This is a retrospective analysis of 87 patients with exudative age-related macular degeneration who received three monthly intravitreal ranibizumab injections. Visual acuity before initiation of intravitreal

therapy and 4-6 weeks after last intravitreal injection was compared and related to the preoperative visualisation of continuity of the outer retinal layers as assessed by OCT: external limiting membrane (ELM), inner photoreceptor segments (IPS), junction between inner and outer segments (IS/OS), and outer photoreceptor segments (OPS).

Results: Visual acuity increased in 40 of 87 (46.0%) patients, it remained stable in 25 (28.7%), and 22 (25.3%) patients had decreased visual acuity four to six weeks after triple intravitreal ranibizumab injections. No statistically significant predictive value could be demonstrated for grade of continuity of outer retinal layers concerning visual acuity development.

Conclusions: In our series of AMD patients, grade of continuity of outer retinal layers was not a significant predictive value for visual acuity development after triple ranibizumab injections.

PMID: 22523654 [PubMed - in process] PMCID: PMC3317217

Acta Ophthalmol. 2012 Apr 20. doi: 10.1111/j.1755-3768.2012.02407.x. [Epub ahead of print]

Assessment of macular pigment optical density in patients with unilateral wet age-related macular degeneration: authors reply.

Tsika C, Tsilimbaris MK, Makridaki M, Kontadakis G, Plainis S, Moschandreas J.

Department of Ophthalmology, Faculty of Medicine, University Hospital of Heraklion, Crete, Heraklion, Greece Institute of Vision & Optics, Faculty of Medicine, School of Health Sciences, University of Crete, Crete, Greece Department of Optometry and Neuroscience, Faculty of Life Sciences, University of Manchester, Manchester, UK Preventive Medicine and Nutrition Clinic, Division of Social Medicine, Faculty of Medicine, School of Health Sciences, University of Crete, Crete, Greece.

PMID: 22520077 [PubMed - as supplied by publisher]

Pathogenesis

Biochim Biophys Acta. 2012 Apr 12. [Epub ahead of print]

αB-crystallin/sHSP protects cytochrome c and mitochondrial function against oxidative stress in sens and retinal cells.

McGreal RS, Kantorow WL, Chauss DC, Wei J, Brennan LA, Kantorow M.

BACKGROUND: αB-crystallin/sHSP protects cells against oxidative stress damage. Here, we mechanistically examined its ability to preserve mitochondrial function in lens and retinal cells and protect cytochrome c under oxidative stress conditions.

METHODS: αB-crystallin/sHSP was localized in human lens (HLE-B3) and retinal (ARPE-19) cells. αB-crystallin/sHSP was stably over-expressed and its ability to preserve mitochondrial membrane potential under oxidative stress conditions was monitored. Interactions between αB-crystallin/sHSP and cytochrome c were examined by fluorescent resonance energy transfer (FRET) and by co-immune precipitation. The ability of αB-crystallin/sHSP to protect cytochrome c against methionine-80 oxidation was monitored.

RESULTS: αB-crystallin/sHSP is present in the mitochondria of lens and retinal cells and is translocated to the mitochondria under oxidative conditions. αB-crystallin/sHSP specifically interacts with cytochrome c in vitro and in vivo and its overexpression preserves mitochondrial membrane potential under oxidative stress conditions. αB-crystallin/sHSP directly protects cytochrome c against oxidation.

GENERAL SIGNIFICANCE: These data demonstrate that αB-crystallin/sHSP maintains lens and retinal

cells under oxidative stress conditions at least in part by preserving mitochondrial function and by protecting cytochrome c against oxidation. Since oxidative stress and loss of mitochondrial function are associated with eye lens cataract and age-related macular degeneration, loss of these αB-crystallin/sHSP functions likely plays a key role in the development of these diseases. αB-crystallin/sHSP is expressed throughout the body and its ability to maintain mitochondrial function is likely important for the prevention of multiple degenerative diseases.

PMID: 22521365 [PubMed - as supplied by publisher]

Int J Inflam. 2012;2012:581695. Epub 2012 Mar 22.

Renin-Angiotensin system hyperactivation can induce inflammation and retinal neural dysfunction.

Kurihara T, Ozawa Y, Ishida S, Okano H, Tsubota K.

Department of Ophthalmology, Keio University School of Medicine, 35 Shinanomachi, Shinjyuku-ku, Tokyo 160-8582, Japan.

Abstract

The renin-angiotensin system (RAS) is a hormone system that has been classically known as a blood pressure regulator but is becoming well recognized as a proinflammatory mediator. In many diverse tissues, RAS pathway elements are also produced intrinsically, making it possible for tissues to respond more dynamically to systemic or local cues. While RAS is important for controlling normal inflammatory responses, hyperactivation of the pathway can cause neural dysfunction by inducing accelerated degradation of some neuronal proteins such as synaptophysin and by activating pathological glial responses. Chronic inflammation and oxidative stress are risk factors for high incidence vision-threatening diseases such as diabetic retinopathy (DR), age-related macular degeneration (AMD), and glaucoma. In fact, increasing evidence suggests that RAS inhibition may actually prevent progression of various ocular diseases including uveitis, DR, AMD, and glaucoma. Therefore, RAS inhibition may be a promising therapeutic approach to fine-tune inflammatory responses and to prevent or treat certain ocular and neurodegenerative diseases.

PMID: 22536545 [PubMed - in process] PMCID: PMC3321303

Ophthalmologica. 2012;227 Suppl 1:2-10. Epub 2012 Apr 24.

Biological, preclinical and clinical characteristics of inhibitors of vascular endothelial growth factors.

Chong V.

Oxford Eye Hospital, Oxford University Hospitals, Headley Way, Oxford, UK.

Abstract

Vascular endothelial growth factor (VEGF) plays an important role in the pathophysiology of several sight-threatening retinal disorders such as age-related macular degeneration, diabetic macular edema and proliferative diabetic retinopathy. The discovery of anti-VEGF agents has revolutionized our treatment of these conditions. There are 4 anti-VEGF agents that are either approved or in common use in ophthalmology, namely pegaptanib (Macugen, Pfizer), ranibizumab (Lucentis, Novartis), aflibercept or VEGF Trap-Eye (EYLEA, Bayer) and bevacizumab (Avastin, Roche). There are differences between them. In this review, the differences are discussed in detail. Furthermore, an attempt is made to explain some of the clinical trial data based on their differences in ocular efficacy, duration of action, and local and systemic safety concerns.

PMID: 22517120 [PubMed - in process]

Methods Mol Biol. 2012;874:55-67.

Immunohistochemical detection of sphingosine-1-phosphate and sphingosine kinase-1 in human tissue samples.

Visentin B, Reynolds G, Sabbadini R.

Lpath Incorporated, San Diego, CA, USA, bvisentin@lpath.com.

Abstract

Sphingosine-1-phosphate (S1P) and the enzyme primarily responsible for its production, sphingosine kinase-1 (SphK-1), are thought to be dysregulated in multiple human diseases including cancer, multiple sclerosis (MS), diabetes, neurological diseases, fibrosis, and certain pathologies associated with impaired angiogenesis such as, age-related macular degeneration (AMD). Antibody-based techniques to identify and localize S1P and SphK-1 within cells and tissue specimens represent powerful tools not only to understand the biological role of these molecules but also to validate these unique in-class targets in multiple state diseases. Consequently, the potential applications of these molecules for therapy and diagnostic purposes are currently under investigation. Here, we describe two staining procedures for identification of S1P and SphK-1 in human frozen tissue samples and the challenges encountered in the process of localization in tissue samples of lipid molecules, such as S1P.

PMID: 22528439 [PubMed - in process]

Biochim Biophys Acta. 2012 Apr 12. [Epub ahead of print]

αB-crystallin/sHSP protects cytochrome c and mitochondrial function against oxidative stress in sens and retinal cells.

McGreal RS, Kantorow WL, Chauss DC, Wei J, Brennan LA, Kantorow M.

BACKGROUND: αB-crystallin/sHSP protects cells against oxidative stress damage. Here, we mechanistically examined its ability to preserve mitochondrial function in lens and retinal cells and protect cytochrome c under oxidative stress conditions.

METHODS: αB-crystallin/sHSP was localized in human lens (HLE-B3) and retinal (ARPE-19) cells. αB-crystallin/sHSP was stably over-expressed and its ability to preserve mitochondrial membrane potential under oxidative stress conditions was monitored. Interactions between αB-crystallin/sHSP and cytochrome c were examined by fluorescent resonance energy transfer (FRET) and by co-immune precipitation. The ability of αB-crystallin/sHSP to protect cytochrome c against methionine-80 oxidation was monitored.

RESULTS: αB-crystallin/sHSP is present in the mitochondria of lens and retinal cells and is translocated to the mitochondria under oxidative conditions. αB-crystallin/sHSP specifically interacts with cytochrome c in vitro and in vivo and its overexpression preserves mitochondrial membrane potential under oxidative stress conditions. αB-crystallin/sHSP directly protects cytochrome c against oxidation.

GENERAL SIGNIFICANCE: These data demonstrate that αB-crystallin/sHSP maintains lens and retinal cells under oxidative stress conditions at least in part by preserving mitochondrial function and by protecting cytochrome c against oxidation. Since oxidative stress and loss of mitochondrial function are associated with eye lens cataract and age-related macular degeneration, loss of these αB-crystallin/sHSP functions likely plays a key role in the development of these diseases. αB-crystallin/sHSP is expressed throughout the body and its ability to maintain mitochondrial function is likely important for the prevention of multiple degenerative diseases.

PMID: 22521365 [PubMed - as supplied by publisher]

Mol Aspects Med. 2012 Apr 10. [Epub ahead of print]

Roles for the ubiquitin-proteasome pathway in protein quality control and signaling in the retina: Implications in the pathogenesis of age-related macular degeneration.

Shang F, Taylor A.

Laboratory for Nutrition and Vision Research, USDA Human Nutrition Research Center on Aging, 711 Washington St., Boston, MA 02111, United States.

Abstract

The accumulation of damaged or postsynthetically modified proteins and dysregulation of inflammatory responses and angiogenesis in the retina/RPE are thought be etiologically related to formation of drusen and choroidal neovascularization (CNV), hallmarks of age-related macular degeneration (AMD). The ubiquitin-proteasome pathway (UPP) plays crucial roles in protein quality control, cell cycle control and signal transduction. Selective degradation of aberrant proteins by the UPP is essential for timely removal of potentially cytotoxic damaged or otherwise abnormal proteins. Proper function of the UPP is thought to be required for cellular function. In contrast, age - or stress induced - impairment the UPP or insufficient UPP capacity may contribute to the accumulation of abnormal proteins, cytotoxicity in the retina, and AMD. Crucial roles for the UPP in eye development, regulation of signal transduction, and antioxidant responses are also established. Insufficient UPP capacity in retina and RPE can result in dysregulation of signal transduction, abnormal inflammatory responses and CNV. There are also interactions between the UPP and lysosomal proteolytic pathways (LPPs). Means that modulate the proteolytic capacity are making their way into new generation of pharmacotherapies for delaying age-related diseases and may augment the benefits of adequate nutrition, with regard to diminishing the burden of AMD.

PMID: 22521794 [PubMed - as supplied by publisher]

Epidemiology

Stroke. 2012 Apr 24. [Epub ahead of print]

Age-Related Macular Degeneration and Long-Term Risk of Stroke Subtypes.

Ikram MK, Mitchell P, Klein R, Sharrett AR, Couper DJ, Wong TY.

From the Singapore Eye Research Institute, Singapore National Eye Centre, Singapore; the. Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; the Department of Ophthalmology, Erasmus Medical Center, Rotterdam, The Netherlands; the Department of Ophthalmology and Westmead Millennium Institute, Centre for Vision Research, University of Sydney, Sydney, Australia; the Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, Madison, WI; the Department of Epidemiology, John Hopkins Bloomberg School of Public Health, Baltimore, MD; and the Department of Biostatistics, University of North Carolina, Chapel Hill, NC.

BACKGROUND AND PURPOSE: We examined the relationship of age-related macular degeneration (AMD) with incident stroke, including stroke subtypes of cerebral infarction and intracerebral hemorrhage.

METHODS: We included 12ü216 participants with retinal photographs taken at the third examination visit (1993-1995) from the Atherosclerosis Risk in Communities (ARIC) Study, a population-based cohort study in middle-aged persons. Images were evaluated for AMD signs according to a standardized protocol. Incident events of stroke and its subtypes were identified and validated through case record review over time.

RESULTS: AMD was diagnosed in 591 participants, of whom 576 had early and 15 late AMD. After a mean

follow-up of 13.0 years (SD, 3.3), 619 persons developed an incident stroke, including 548 cerebral infarction and 57 intracerebral hemorrhages. Participants with any AMD were at an increased risk of stroke (multivariable adjusted hazard ratio, 1.51; 95% CI, 1.11-2.06) with a stronger association for intracerebral hemorrhage (hazard ratio, 2.64; 95% CI, 1.18-5.87) than cerebral infarction (hazard ratio, 1.42; 95% CI, 1.01-1.99).

CONCLUSIONS: Persons with AMD are at an increased risk of both cerebral infarction and intracerebral hemorrhage. These data provide further insight into common pathophysiological processes between AMD and stroke subtypes.

PMID: 22535267 [PubMed - as supplied by publisher]

Ophthalmology. 2012 Apr 24. [Epub ahead of print]

Validity of Self-reported Eye Disease and Treatment in a Population-based Study: The Los Angeles Latino Eye Study.

Patty L, Wu C, Torres M, Azen S, Varma R; Los Angeles Latino Eye Study Group.

Doheny Eye Institute and the Department of Ophthalmology, Keck School of Medicine, University of Southern California, Los Angeles, California.

PURPOSE: To examine the validity of self-reported eye disease, including cataract, age-related macular degeneration (AMD), glaucoma, and diabetic retinopathy (DR), and self-reported surgical treatment for cataract and DR in the Los Angeles Latino Eye Study (LALES).

DESIGN: Population-based, cross-sectional study.

PARTICIPANTS: A total of 6357 Latinos aged 40+ years from the LALES.

METHODS: Participants underwent a detailed interview, including survey questions about ocular health, diagnoses, and timing of last eye examination, and a standardized clinical examination. Self-report was compared with examination to determine sensitivity and specificity by length of time since last eye examination. Stepwise logistic regression was used to determine factors associated with inaccurate self-report.

MAIN OUTCOME MEASURES: Sensitivity and specificity were calculated for 4 self-reported eye diseases (cataract, AMD, glaucoma, and DR) and for surgical treatment of cataract and DR. Odds ratios (ORs) were determined for factors associated with inaccurate self-report underestimating eye disease and treatment.

RESULTS: For each disease, sensitivity and specificity in those who reported their last eye examination as <1 year ago were 36.8% and 92.5% for cataract, 37.7% and 96.3% for glaucoma, 5.1% and 98.9% for AMD, and 25.7% and 94.2% for DR, respectively. Self-report was less accurate with increasing time since last eye examination. Inaccurate self-report was independently associated with better visual acuity (OR, 2.4), <2 comorbidities (OR, 1.7), last eye examination/visit 1 to 5 years ago and ≥5 years ago (OR, 2.3 and 4.9, respectively), and less education (OR, 1.3 for 7-12 years and 1.7 for <7 years). Of 88 participants surgically treated for cataract who reported an eye examination <1 year ago, sensitivity and specificity of self-reported surgical history were 90.9% and 99.9%, respectively. Of the 31 participants treated for DR (laser/surgery) and reporting an eye examination <1 year ago, sensitivity and specificity of self-reported surgical history were 19.4% and 99.6%, respectively.

CONCLUSIONS: Among Latinos, self-reporting of eye disease and surgical history provides a significant underestimate of the disease burden. This may lead to significant misclassification in vision research if self-report alone is used to identify persons with eye disease.

PMID: 22537615 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2012;6:561-4. Epub 2012 Apr 11.

Is age-related macular degeneration a problem in Ibadan, Sub-Saharan Africa?

Oluleye TS.

Retina and Vitreous Unit, Department of Ophthalmology, University College Hospital, Ibadan, Nigeria, West Africa.

BACKGROUND: Age-related macular degeneration (AMD) is considered uncommon in black populations including those of Sub-Saharan Africa. The aim of this review was to determine the pattern of presentation of AMD in our hospital located in Ibadan, the largest city in Sub-Saharan Africa.

METHODS: A retrospective review of all cases with AMD presenting to the Eye and Retinal Clinic of the University College Hospital, Ibadan, West Africa was undertaken between October 2007 and September 2010.

RESULTS: In the 3 years reviewed, 768 retinal cases were seen in the hospital, 101 (14%) of which were diagnosed with AMD. The peak age was 60-79 years. The male to female ratio was approximately 2:3. More males presented with the advanced form of dry AMD than females (odds ratio = 2.33). However, more females had advanced wet AMD than males (odds ratio = 1.85). Wet AMD was seen in 40 cases (40%).

CONCLUSION: The review determined that, as AMD is not uncommon and wet AMD is relatively more common in our hospital than has been reported previously, this is probably true of Ibadan in general.

PMID: 22536053 [PubMed - in process] PMCID: PMC3334226

Ophthalmologe. 2012 Apr;109(4):369-76.

[Blindness in Germany - comparison between retrospective data and predictions for the future].

[Article in German]

Rohrschneider K.

Ophthalmologische Rehabilitation, Augenklinik, Universitätsklinikum Heidelberg, Im Neuenheimer Feld 400, 69120, Heidelberg, Deutschland, kr@uni-hd.de.

AIM: There are no exact figures on the number of blind and visually impaired persons in Germany. The purpose of this study was to compare the development over the last years with earlier predictions and an outlook into the future.

METHODS: Data from scientific publications as well as the Federal Statistical Office and from organizations for the blind on the frequency of blindness was compared to the forecast development of blindness. In addition the development of the frequency of age-related macular degeneration (ARMD) was taken into consideration.

RESULTS: While the proportion of over 60-year-olds has steadily increased from 21% in 1993 to 25.9% in 2009, the ratio of blind people has risen from 8.9 per 10,000 inhabitants in 1993 to 10.6 per 10,000 inhabitants in 2003. However, up to 2009 decreased every year to 9.7 which is approximately the same as 1995, although ARMD has also become much more frequent as the main cause. Additionally there are considerable differences up to a factor two between the various studies on the number of blind people in different regions of Germany.

DISCUSSION: At present there are approximately 150,000 blind and about 500,000 visually impaired persons in Germany. However, these numbers are only on the basis of estimates and according to studies in other European nations. Similar uncertainty exists concerning the diseases causing blindness. A transfer

from epidemiological studies is limited especially because of the different definition of blindness. The expected increase of visually impaired and blind persons for the last 20 years as a result of the increasing age cannot be confirmed from the present data. It would be desirable to extensively register the specifications to prevalence and incidence of visual impairment and blindness including valid information on the corresponding cause to confirm the rising importance of visual impairment.

PMID: 22527735 [PubMed - in process]

Genetics

Ophthalmology. 2012 Apr 20. [Epub ahead of print]

Role of Vascular Endothelial Growth Factor Polymorphisms in the Treatment Success in Patients with Wet Age-related Macular Degeneration.

Boltz A, Ruiβ M, Jonas JB, Tao Y, Rensch F, Weger M, Garhöfer G, Frantal S, El-Shabrawi Y, Schmetterer L.

Department of Clinical Pharmacology, Medical University of Vienna, Vienna, Austria; Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria.

PURPOSE: Along with environmental risk factors such as smoking, hypertension, and atherosclerosis, genetic susceptibility is a primary contributor to the development and progression of exudative age-related macular degeneration (AMD). Vascular endothelial growth factor (VEGF) is a central angiogenic regulator and there has been general agreement now that it is an important trigger for the progression of exudative AMD. In the present study, we tested the hypothesis that VEGF gene polymorphisms play a role in the treatment success with VEGF inhibitors in patients with exudative AMD.

DESIGN: Prospective cohort study.

PARTICIPANTS: We included 185 eyes of 141 patients with exudative AMD who were scheduled for their first treatment with intravitreally administered bevacizumab in this trial.

METHODS: All patients were aged >50 years and had angiographically verified exudative AMD. Blood from the finger pad was collected on blood cards for genotyping for the VEGF polymorphisms rs1413711, rs3025039, rs2010963, rs833061, rs699947, rs3024997, and rs1005230. At each follow-up visit, visual acuity was reassessed and an ophthalmic examination was carried out. Visual acuity outcome, number of retreatments, and overall time of treatment were analyzed in dependence of the VEGF polymorphisms.

MAIN OUTCOME MEASURES: Mean change in visual acuity at the end of the treatment period.

RESULTS: The included patients were reinjected with bevacizumab 1 to 15 times, resulting in a total treatment period of 42 to 1182 days. In univariate analysis only the G/G genotypes of rs3024997 and rs2010963 compared with all other 5 single nucleotide polymorphisms (SNPs) showed a significantly lower visual acuity at the end of treatment. In multivariate analysis including parameters such as time, baseline visual acuity, and number of reinjections, none of the SNPs showed a significant correlation.

CONCLUSIONS: The current study indicates that VEGF polymorphisms are not major predictors of anti-VEGF treatment success in patients with exudative AMD.

PMID: 22521084 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2012;6:465-71. Epub 2012 Mar 22.

Major single nucleotide polymorphisms in polypoidal choroidal vasculopathy: a comparative analysis between Thai and other Asian populations.

Chantaren P, Ruamviboonsuk P, Ponglikitmongkol M, Tiensuwan M, Promso S.

Department of Ophthalmology, Rajavithi Hospital, Bangkok.

PURPOSE: To investigate the association in a Thai population between the major age-related macular degeneration (AMD) susceptibility loci, Y402H and I62V in the complement factor H (CFH) and A69S in the age-related maculopathy susceptibility 2 (ARMS2) genes, and polypoidal choroidal vasculopathy (PCV).

METHODS: A case-control study included 97 PCV cases and 102 age- and gender-matched controls without any retinopathy. The genotypic profiles of the three polymorphisms were obtained using a real-time polymerase chain reaction assay. The allelic and genotypic association between the polymorphisms and PCV were compared with those from the compiled data of other Asian populations reported previously.

RESULTS: Strong associations between the Y402H, I62V, and A69S polymorphisms and PCV were observed in the present study (P = 0.002, 0.003, and 0.0008 respectively) and in the compiled data (P < 0.0001 for all three polymorphisms). The risk allele frequencies of the polymorphisms in PCVs and in controls from the present study (15.0% and 5.4% for Y402H, 71.7% and 57.4% for I62V, and 54.1% and 37.3% for A69S respectively) were also comparable with the frequencies from the compiled data (10.3% and 6.4% for Y402H, 75.2% and 58.3% for I62V, and 56.8% and 36.8% for A69S respectively). The genotype distribution for each polymorphism was also comparable in both datasets.

CONCLUSION: The findings of this study support a significant genetic association between the major AMD susceptibility genes and PCV across Asian populations. This suggests that AMD and PCV, despite different phenotypic manifestation, may share common genetic risk factors.

PMID: 22536038 [PubMed - in process] PMCID: PMC3334218