Macular Disease Foundation AUSTRALIA
Our focus is your vision

MD Research News

Issue 211

Tuesday 16 December, 2014

This free weekly bulletin lists the latest published research articles on macular degeneration (MD) and some other macular diseases as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases.

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

Graefes Arch Clin Exp Ophthalmol. 2014 Dec 11. [Epub ahead of print]

Rate of vision loss in neovascular age-related macular degeneration explored.

Real JP, Granero GE, De Santis MO, Juarez CP, Palma SD, Kelly SP, Luna JD.

PURPOSE: To explore decline in visual acuity in patients with neovascular age-related macular degeneration (n-AMD) awaiting intravitreal bevacizumab or ranibizumab treatment following initial diagnosis and after disease reactivation.

METHODS: Retrospective analysis of 74 treatment-naïve patients (84 eyes) in two centers in Córdoba, Argentina. The time between treatment indication and intravitreal injection, and the changes in BCVA produced during this delay were studied in both periods. A linear regression model to search the impact of time on progression visual impairment was conducted.

RESULTS: In both periods, a significant reduction in vision occurred awaiting intravitreal injection. The longer the delay, the greater the vision loss ($R2 = 0.55$ $p < 0.01$) and the less improvement following treatment (Pearson coefficient -0.26). The result of the model shows that the change in vision as a function of initial delay were best described by a polynomic model with a mean loss of 5 letters in the first 3 weeks, a slowdown in the rate of change of VA, and a dependence of visual acuity at the moment of diagnosis . The loss of visual acuity after reactivation shows the same behavior as at the onset of the disease but independent of visual acuity prior to reactivation.

CONCLUSION: Visual loss awaiting injection intravitreal anti-VEGF is clinically significant and with an asymptotic pattern, with early rapid loss of vision in both the onset of the disease and the reactivation. Initiation of anti-VEGF treatment must be undertaken urgently, as should retreatment of disease activation to reduce visual loss.

PMID: 25491161 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2014 Dec 8. [Epub ahead of print]

Systemic levels of vascular endothelial growth factor before and after intravitreal injection of aflibercept or ranibizumab in patients with age-related macular degeneration: a randomised, prospective trial.

Zehetner C, Kralinger MT, Modi YS, Waltl I, Ulmer H, Kirchmair R, Bechrakis NE, Kieselbach GF.

PURPOSE: To evaluate the changes of vascular endothelial growth factor (VEGF) plasma levels after intravitreal injections of aflibercept or ranibizumab in patients with exudative age-related macular degeneration (AMD).

METHODS: Thirty-eight patients with exudative AMD were included in this randomised, prospective study. Nineteen patients were randomised to treatment with intravitreal aflibercept (2.0 mg) and 19 to intravitreal ranibizumab (0.5 mg). The concentration of VEGF was measured by ELISA just before the injection, after 7 days and 1 month. Twenty-two age- and sex-matched healthy patients without chorioretinal diseases served as control.

RESULTS: The median baseline plasma VEGF concentration was 61.0 pg/ml in the control group, 43.0 pg/ml in the aflibercept group and 59.0 pg/ml in the ranibizumab group ($p = 0.127$). Seven days after intravitreal injection of aflibercept plasma levels were significantly reduced to values below the minimum detectable dose (MDD) in 17 of 19 patients (89.5%) resulting in a median VEGF concentration of <9 pg/ml ($p < 0.001$). The reduction persisted throughout 1 month with values below the MDD in 5 of 19 patients (26.3%) and a median measurement of 17.0 pg/ml ($p < 0.001$). In patients treated with ranibizumab no significant effects could be observed with a baseline VEGF of 59.0 pg/ml, 54.0 pg/ml at 7 days ($p = 0.776$) and 58.5 pg/ml at 4 weeks of follow-up ($p = 0.670$).

CONCLUSION: After intravitreal aflibercept injection, the systemic VEGF levels were significantly reduced throughout the observational period of 4 weeks. No significant systemic effects of intravitreal ranibizumab on plasma VEGF were observed.

PMID: 25488124 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2014 Dec 9. [Epub ahead of print]

A prospective, observational, open-label, multicentre study to investigate the daily treatment practice of ranibizumab in patients with neovascular age-related macular degeneration.

van Asten F, Evers-Birkenkamp KU, van Lith-Verhoeven JJ, de Jong-Hesse Y, Hoppenreijs VP, Hommersom RF, Scholten AM, Hoyng CB, Klaver JH; the HELIOS study group.

PURPOSE: The HELIOS (Health Economics with Lucentis in Observational Settings) study was designed on request of the Dutch Health Authority for an observational study to assess the effectiveness and safety of ranibizumab for neovascular age-related macular degeneration (wet AMD) in daily practice.

METHODS: The HELIOS study was a 2-year prospective, observational, open-label, multicentre study involving 14 sites. Patients with wet AMD were enrolled and observed for a period of 24 months. The data were collected at baseline and at the visits closest around the time-points 3, 6, 12, 18 and 24 months after inclusion.

RESULTS: Treatment with ranibizumab resulted in prevention of vision loss. The mean ETDRS score increased from 45.1 letters at baseline to 48.5 letters at 24 months. This was achieved with a mean of 7.8 injections over 24 months. Stabilization of visual acuity was also reflected by the scores on the quality of life EQ-5D questionnaire, which did not significantly change over the study period. The more subjective EQ-VAS questionnaire showed an overall improvement. The VFQ-25 questionnaire was also mostly stable over time. After 24 months, 32.2% of the patients gained ≥1 letter and 17.1% gained >15 letters. Patients completing the loading phase were better responders, as demonstrated by increased long-term visual acuity. In addition, ranibizumab was well tolerated and had a safety profile commonly seen in routine clinical practice.

CONCLUSION: This study demonstrates that also in daily practice ranibizumab was effective in preventing vision loss over a period of 24 months. No new safety findings were identified.

PMID: 25488348 [PubMed - as supplied by publisher]

Expert Opin Drug Saf. 2014 Dec 9:1-10. [Epub ahead of print]

Systemic safety of anti-VEGF drugs: a commentary.

Scott LJ, Chakravarthy U, Reeves BC, Rogers CA.

Introduction: VEGF is a mediator of angiogenesis. Thus, concerns have been expressed following the use of VEGF inhibitors for the treatment of neovascular age-related macular degeneration (nAMD). Ranibizumab, and more recently aflibercept, are VEGF inhibitors licensed for the treatment of nAMD. Bevacizumab is also used but unlicensed for this application.

Areas covered: A non-systematic review of nAMD trials was undertaken to investigate four outcomes: all-cause mortality, all systemic serious adverse events (SSAEs), arteriothrombotic events (ATEs) and gastrointestinal (GI) complications. Differences in event rates with injections of ranibizumab compared to bevacizumab, aflibercept, photodynamic therapy (PDT) and sham were explored and quantified using fixed-effect meta-analyses.

Expert opinion: Anti-VEGF agents can influence vascular health; however, the data suggest no difference in the risk of an ATE or death between anti-VEGF agents. Clinical trials are limited in their size and eligibility criteria and databases of patients treated in routine practice should also be scrutinized.

PMID: 25489638 [PubMed - as supplied by publisher]

Expert Rev Clin Pharmacol. 2015 Jan;8(1):135-40.

Current choice of treatments for neovascular AMD.

Lai K, Landa G.

Abstract: Age-related macular degeneration is the leading cause of irreversible blindness in developed countries with the neovascular form accounting for the majority of severe vision loss in the disease. The management of wet age-related macular degeneration has improved drastically in the past decade as anti-VEGF agents took its place at the forefront of treatment. As the choice of therapy is based on a number of factors, this review summarizes the pivotal studies that brought these agents to use and compares the different agents currently available. This review also briefly describes the promising new therapies that are in development.

PMID: 25487081 [PubMed - in process]

Graefes Arch Clin Exp Ophthalmol. 2014 Dec 6. [Epub ahead of print]

Reply to the letter to the editor: bimonthly injections of ranibizumab for age-related macular degeneration.

Sawada T, Ohji M.

PMID: 25480718 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2014 Dec 9. [Epub ahead of print]

Clinical characteristics and outcomes after 5 years pro re nata treatment of neovascular age-related macular degeneration with ranibizumab.

Airody A, Venugopal D, Allgar V, Gale RP.

PMID: 25488611 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2014 Dec 9. [Epub ahead of print]

Bimonthly injections of ranibizumab for age-related macular degeneration.

Ilhan A, Tas A, Yolcu U, Gundogan FC.

PMID: 25488573 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Medicina (Kaunas). 2014;50(5):281-6. Epub 2014 Nov 1.

A new maximum color contrast sensitivity test for detecting early changes of visual function in age-related macular degeneration.

Liutkevičienė R, Cebatorienė D, Zaliūnienė D, Lukauskienė R, Jašinskas V.

BACKGROUND AND OBJECTIVE: To determine the association between age-related macular degeneration (AMD) and color perception established by the Farnsworth-Munsell 100 hue (F-M 100) and maximum color contrast sensitivity (MCCS) tests.

MATERIALS AND METHODS: We performed a case-control study, which comprised of 100 patients with AMD and 100 healthy controls. To test visual acuity (VA), a typical Snellen chart was used. The computerized F-M 100 and MCCS programs were used for color discrimination.

RESULTS: The results of VA, and the F-M 100 and MCCS tests in the healthy controls were statistically significantly better than in the patients with AMD (1.0 vs. 0.82±0.16, P=0.005; 87.39±24.11 vs. 185.39±74.43, P=0.005; 1.33±1.17 vs. 1.96±0.46, P=0.005, respectively). When VA was 1.0 in patients with AMD, the total error scores of the F-M 100 test and MCCS test compared with healthy persons were even worse (166.09±66.57 vs. 87.39±24.11, P=0.002; 1.67±0.92 vs. 1.33±1.17, P=0.001, respectively). Analysis of the results of patients with AMD compared to healthy controls showed the highest error score in the blue color range.

CONCLUSIONS: The results of the color contrast sensitivity test decreased by half in patients with AMD compared with ophthalmologically healthy patients when they performed the F-M 100 test and by one and half when they performed a MCCS test in the blue color range.

PMID: 25488164 [PubMed - in process]

Arq Bras Oftalmol. 2014 Oct;77(5):315-320. Epub 2014 Sep 1.

Grid laser photocoagulation in the treatment of serous avascular pigment epithelial detachment in age-related macular degeneration.

Zago Filho LA, Moreira AT, Malafaia O, Matias JE.

Purpose: Describe the outcomes of thermal laser photocoagulation in three cases of retinal pigment epithelium detachment associated to age-related macular degeneration.

Methods: Three patients with avascular retinal pigment epithelium detachment were treated with green diode laser photocoagulation. Mild macular grid laser application, similar to the treatment of diabetic macular edema was performed after an unsuccessful intravitreal anti-angiogenic treatment.

Results: After one year of the laser treatment, two cases reached anatomic resolution, with complete absorption of sub-epithelium serum fluid and improvement of the visual acuity. There was stability of the visual acuity and sub-epithelium fluid reduction, which, however, was partial in the third case. No

complications related to the treatment occurred until the conclusion of this study.

Conclusions: Macular photocoagulation in grid pattern produced regression of avascular serous pigment epithelium detachment associated with age-related macular degeneration in a short follow-up period. Although long term prospective studies with an increased sample are necessary, it is a method that can be applied in selected patients, with absence of sub-retinal neovascularization or sub-epithelium fibrovascular component.

PMID: 25494379 [PubMed - as supplied by publisher]

Pathogenesis

BMC Ophthalmol. 2014 Dec 8;14(1):154. [Epub ahead of print]

Prevalence of anti-retinal autoantibodies in different stages of Age-related macular degeneration.

Adamus G, Chew EY, Ferris FL, Klein ML.

BACKGROUND: Age-related macular degeneration (AMD) is the leading cause of central vision loss in older adults. Anti-retinal autoantibodies (AAbs) have been found in individuals with AMD. The goal of the study was to determine the AAb specificity in different stages of AMD, and determine whether there is a prevalent AAb signature.

METHODS: Sera of 134 participants in the Age-related Eye Disease Study were analyzed for anti-retinal AAbs by western blotting. The subjects were classified by diagnostic subgroups based upon their clinical classification: No AMD, Intermediate AMD, and Late AMD - geographic atrophy (GA) and Late AMD - neovascular (NV).

RESULTS: The presence of anti-retinal AAb was detected in 58% patients with Intermediate and Late AMD, and 54% of those with no AMD. AAbs bound to fifteen different retinal antigens. Most individuals had 1 specific AAbs (67%), with the remainder having 2 to 4 different AAbs. Over 40% of patients with Intermediate AMD, and 46% of those with GA had anti-enolase AAbs, compared with 29% of individuals with NV and 29% with no AMD. Different AAbs signatures related to NV as compared to GA and/or Intermediate AMD were distinguished. Anti-40-kDa (10%) and 42-kDa (16%) autoantibodies were associated with Intermediate AMD, while anti-30-kDa AAbs (23%) were primarily present in GA. Anti-32-kDa (12%), 35-kDa (21%), and 60-kDa (8%) AAbs were more frequent in NV AMD.

CONCLUSIONS: A unique AAb pattern for each of the disease subgroups was present when AMD progressed from the intermediate to the late forms of severity. Differences in the frequency of specific AAbs between AMD subgroups suggested that they may participate in pathogenicity of AMD. Further studies are necessary to confirm these observations in the larger cohort and individual AMD patients over time.

PMID: 25488058 [PubMed - as supplied by publisher]

PLoS One. 2014 Dec 10;9(12):e114964.

Induction of Covalently Crosslinked p62 Oligomers with Reduced Binding to Polyubiquitinated Proteins by the Autophagy Inhibitor Verteporfin.

Donohue E, Balgi AD, Komatsu M, Roberge M.

Abstract: Autophagy is a cellular catabolic process responsible for the degradation of cytoplasmic constituents, including organelles and long-lived proteins, that helps maintain cellular homeostasis and protect against various cellular stresses. Verteporfin is a benzoporphyrin derivative used clinically in photodynamic therapy to treat macular degeneration. Verteporfin was recently found to inhibit

autophagosome formation by an unknown mechanism that does not require exposure to light. We report that verteporfin directly targets and modifies p62, a scaffold and adaptor protein that binds both polyubiquitinated proteins destined for degradation and LC3 on autophagosomal membranes. Western blotting experiments revealed that exposure of cells or purified p62 to verteporfin causes the formation of covalently crosslinked p62 oligomers by a mechanism involving low-level singlet oxygen production. Rose bengal, a singlet oxygen producer structurally unrelated to verteporfin, also produced crosslinked p62 oligomers and inhibited autophagosome formation. Co-immunoprecipitation experiments demonstrated that crosslinked p62 oligomers retain their ability to bind to LC3 but show defective binding to polyubiquitinated proteins. Mutations in the p62 PB1 domain that abolish self-oligomerization also abolished crosslinked oligomer formation. Interestingly, small amounts of crosslinked p62 oligomers were detected in untreated cells, and other groups noted the accumulation of p62 forms with reduced SDS-PAGE mobility in cellular and animal models of oxidative stress and aging. These data indicate that p62 is particularly susceptible to oxidative crosslinking and lead us to propose a model whereby oxidized crosslinked p62 oligomers generated rapidly by drugs like verteporfin or over time during the aging process interfere with autophagy.

PMID: 25494214 [PubMed - as supplied by publisher]

Retina. 2014 Dec 9. [Epub ahead of print]

DIFFERENTIAL EXPRESSION OF VASCULAR ENDOTHELIAL GROWTH FACTOR-A ISOFORMS IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

Grisanti S, Zhu Q, Tatar O, Lueke J, Lueke M, Tura A, Grisanti S.

PURPOSE: To investigate the role of vascular endothelial growth factor-A (VEGF-A) isoforms in neovascular age-related macular degeneration.

METHODS: Choroidal neovascular membranes (CNV) were excised in 24 patients, 8 of them underwent previous photodynamic therapy. All procedures were performed before anti-VEGF therapies were implemented in Germany. Normal human donor eyes served as controls. Messenger RNA expression of total VEGF-A and VEGF-A isoforms was measured.

RESULTS: Vascular endothelial growth factor-A121 is the most abundant isoform in CNV and control tissues. In controls, VEGF-A121 is lowest in neural retina and highest in choroids. For total VEGF-A and VEGF-A165, this is vice versa. VEGF-A165 and VEGF-A189 are significantly higher in CNV than in control choroids, the opposite is found for VEGF-A121. After photodynamic therapy, total VEGF-A and VEGF-A121 are increased, VEGF-A165 and VEGF-A189 are decreased. Age-dependently, there is an increase in VEGF-A165 and a decrease in VEGF-A121.

CONCLUSION: Vascular endothelial growth factor-A isoforms are differentially distributed, suggesting that tissue-specific regulation of various isoforms is physiologically important. The disruption of this homeostasis in CNV membranes may be significant in the onset and progression of neovascular age-related macular degeneration. Our findings support the dominant role of VEGF-A121 in neovascular age-related macular degeneration but hint that VEGF-A165 may have an equivalent role in other neovascular retinal pathology.

PMID: 25494018 [PubMed - as supplied by publisher]

Molecules. 2014 Dec 8;19(12):20557-20569.

Role of Protease-Inhibitors in Ocular Diseases.

Pescosolido N, Barbato A, Pascarella A, Giannotti R, Genzano M, Nebbioso M.

Abstract: It has been demonstrated that the balance between proteases and protease-inhibitors system

plays a key role in maintaining cellular and tissue homeostasis. Indeed, its alteration has been involved in many ocular and systemic diseases. In particular, research has focused on keratoconus, corneal wounds and ulcers, keratitis, endophthalmitis, age-related macular degeneration, Sorsby fundus dystrophy, loss of nerve cells and photoreceptors during optic neuritis both in vivo and in vitro models. Protease-inhibitors have been extensively studied, rather than proteases, because they may represent a therapeutic approach for some ocular diseases. The protease-inhibitors mainly involved in the onset of the above-mentioned ocular pathologies are: α2-macroglobulin, α1-proteinase inhibitor (α1-PI), metalloproteinase inhibitor (TIMP), maspin, SERPINA3K, SERPINB13, secretory leukocyte protease inhibitor (SLPI), and calpeptin. This review is focused on the several characteristics of dysregulation of this system and, particularly, on a possible role of proteases and protease-inhibitors in molecular remodeling that may lead to some ocular diseases. Recently, researchers have even hypothesized a possible therapeutic effect of the protease-inhibitors in the treatment of injured eye in animal models.

PMID: 25493637 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2014 Dec 9. [Epub ahead of print]

Intravitreal Autologous Bone Marrow CD34+ Cell Therapy For Ischemic and Degenerative Retinal Disorders: Preliminary Phase 1 Clinical Trial Findings.

Park SS, Bauer G, Abedi M, Pontow S, Panorgias A, Jonnal RS, Zawadzki RJ, Werner JS, Nolta J.

Purpose: Because human bone marrow (BM) CD34+ stem cells home into damaged tissue and may play an important role in tissue repair, this pilot clinical trial explored the safety and feasibility of intravitreal autologous CD34+ BM cells as potential therapy for ischemic or degenerative retinal conditions.

Methods: This prospective study enrolled six subjects (six eyes) with irreversible vision loss from retinal vascular occlusion, hereditary or non-exudative age-related macular degeneration, or retinitis pigmentosa. CD34+ cells were isolated under Good Manufacturing Practice-conditions from the mononuclear cellular fraction of the BM aspirate using a CliniMACs magnetic cell sorter. After intravitreal CD34+ cell injection, serial ophthalmic examinations, microperimetry/perimetry, fluorescein angiography, electroretinography (ERG), optical coherence tomography (OCT), and adaptive optics-OCT were performed during the six-month follow-up.

Results: A mean of 3.4 million (range 1 to 7 million) CD34+ cells were isolated and injected per eye. The therapy was well-tolerated with no intraocular inflammation or hyper-proliferation. Best-corrected visual acuity and full-field ERG showed no worsening after six months. Clinical examination also showed no worsening during follow-up except among AMD subjects where mild progression of geographic atrophy was noted in both the study eye and contralateral eye at six-month follow-up, concurrent with some possible decline on multifocal ERG and microperimetry. Cellular in-vivo imaging using adaptive optics-OCT showed changes suggestive of new cellular incorporation into the macula of hereditary macular degeneration study eye.

Conclusions: Intravitreal autologous BM CD34+ cell therapy appears feasible and well-tolerated in eyes with ischemic or degenerative retinal conditions and merits further exploration.

PMID: 25491299 [PubMed - as supplied by publisher]

Prog Retin Eye Res. 2014 Dec 5. [Epub ahead of print]

Complement Activation and Choriocapillaris Loss in Early AMD: Implications for Pathophysiology and Therapy.

Whitmore SS, Sohn EH, Chirco KR, Drack AV, Stone EM, Tucker BA, Mullins RF.

Abstract: Age-related macular degeneration (AMD) is a common and devastating disease that can result in severe visual dysfunction. Over the last decade, great progress has been made in identifying genetic variants that contribute to AMD, many of which lie in genes involved in the complement cascade. In this review we discuss the significance of complement activation in AMD, particularly with respect to the formation of the membrane attack complex in the aging choriocapillaris. We review the clinical, histological and biochemical data that indicate that vascular loss in the choroid occurs very early in the pathogenesis of AMD, and discuss the potential impact of vascular dropout on the retinal pigment epithelium, Bruch's membrane and the photoreceptor cells. Finally, we present a hypothesis for the pathogenesis of early AMD and consider the implications of this model on the development of new therapies.

PMID: 25486088 [PubMed - as supplied by publisher]

Autophagy. 2014 Oct 30:e36184. [Epub ahead of print]

Dysregulated autophagy in the RPE is associated with increased susceptibility to oxidative stress and AMD.

Mitter S, Song C, Qi X, Mao H, Rao H, Akin D, Lewin A, Grant M, Dunn Jr WA, Ding J, Bowes Rickman C, Boulton ME.

Abstract: Autophagic dysregulation has been suggested in a broad range of neurodegenerative diseases including age-related macular degeneration (AMD). To test whether the autophagy pathway plays a critical role to protect retinal pigmented epithelial (RPE) cells against oxidative stress, we exposed ARPE-19 and primary cultured human RPE cells to both acute (3 and 24 h) and chronic (14 days) oxidative stress and monitored autophagy by western blot, PCR and autophagosome counts in the presence or absence of autophagy modulators. Acute oxidative stress led to a marked increase in autophagy in the RPE whereas autophagy was reduced under chronic oxidative stress. Upregulation of autophagy by rapamycin decreased oxidative stress-induced generation of reactive oxygen species (ROS), whereas inhibition of autophagy by 3-methyladenine (3-MA) or by knockdown of ATG7 or BECN1 increased ROS generation, exacerbated oxidative stress-induced reduction of mitochondrial activity, reduced cell viability and increased lipofuscin. Examination of control human donor specimens and mice demonstrated an age-related increase in autophagosome numbers and expression of autophagy proteins. However, autophagy proteins, autophagosomes and autophagy flux were significantly reduced in tissue from human donor AMD eyes and 2 animal models of AMD. In conclusion, our data confirm that autophagy plays an important role in protection of the RPE against oxidative stress and lipofuscin accumulation and that impairment of autophagy is likely to exacerbate oxidative stress and contribute to the pathogenesis of AMD.

PMID: 25484094 [PubMed - as supplied by publisher]

Cell Cycle. 2014 Nov 15;13(22):3499-3505.

The mitochondria-targeted antioxidant SkQ1 restores αB-crystallin expression and protects against AMD-like retinopathy in OXYS rats.

Muraleva NA, Kozhevnikova OS, Zhdankina AA, Stefanova NA, Karamysheva TV, Fursova AZ, Kolosova NG.

Abstract: Age-related macular degeneration (AMD), a neurodegenerative and vascular retinal disease, is the leading cause of blindness in the developed world. Accumulating evidence suggests that alterations in the expression of a small heat shock protein (αB-crystallin) are involved in the pathogeneses of AMD. Here we demonstrate that senescence-accelerated OXYS rats-an animal model of the dry form of AMD-develop spontaneous retinopathy against the background of reduced expression of αB-crystallin in the retina at the early preclinical stages of retinopathy (age 20 days) as well as at 4 and 24 months of age, during the

progressive stage of the disease. The level of αA-crystallin expression in the retina of OXYS rats at all the ages examined was no different from that in disease-free Wistar rats. Treatment with the mitochondria-targeted antioxidant SkQ1 (plastoquinonyl-decyltriphenylphosphonium) from 1.5 to 4 months of age, 250 nmol/kg, increased the level of αB-crystallin expression in the retina of OXYS rats. SkQ1 slowed the development of retinopathy and reduced histological aberrations in retinal pigment epithelium cells. SkQ1 also attenuated neurodegenerative changes in the photoreceptors and facilitated circulation in choroid blood vessels in the retina of OXYS rats; this improvement was probably linked with the restoration of αB-crystallin expression.

PMID: 25483086 [PubMed - as supplied by publisher]

Mol Med Rep. 2014 Dec 4. [Epub ahead of print]

Effect of charred Radix et Rhizoma Rhei in a laser-induced choroidal neovascularization murine model.

Han D, Yao Y, Sun Y, Gong Y, Wu X.

Abstract: A pharmaceutical composition (patent no. WO2012079419) exhibited favorable outcomes in a clinical trial of wet age‑related macular degeneration. The aims of the present study were to explore the effects of one composition component, charred Radix et Rhizoma Rhei (CRRR), in a laser‑induced choroidal neovascularization (CNV) murine model. A total of 30 eight‑week‑old C57BL/6 mice were subjected to diode laser treatment, and CNV was induced by rupturing the Bruch's membrane. The mice were then randomly divided into two groups: the CRRR‑treated group that was administered CRRR water extract (concentration, 0.6 g/100 ml; dose, 1 ml/0.1 kg twice a day for 21 days); and the control group that was treated with saline (dose, 1 ml/0.1 kg twice a day for 21 days). The retinal tissue was subjected to quantitative polymerase chain reaction (qPCR) and western blot analysis to determine the expression levels of interleukin‑10 (IL‑10) and vascular epithelial growth factor (VEGF) at day seven following laser treatment. At weeks 2 and 3 after laser treatment, fundus fluorescein angiography was performed and graded to assess the severity of lesion leakage. Retinal flat mounts were prepared for three‑dimensional confocal microscopy at day 22 after laser treatment. At days 14 and 21 after laser treatment, no statistically significant differences were observed between the clinically relevant lesions of the CRRR‑treated and control mice. CNV volumes were not found to be significantly different between the CRRR‑treated and control mice. The expression levels of IL‑10 were significantly increased in the CRRR‑treated mice ($P<0.05$). However, no statistically significant differences were observed between the VEGF expression levels of the CRRR‑treated and control mice. In conclusion, CRRR did not appear to significantly inhibit CNV in this murine model. The function of CRRR in the pharmaceutical composition may be due to the effects of IL‑10 and a synergistic effect with other components of the composition. However, further investigation is required.

PMID: 25482457 [PubMed - as supplied by publisher]