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Drug treatment


Combinatorial treatment with topical NSAIDs and anti-VEGF for age-related macular degeneration, a meta-analysis.

Li S, Hu A, Wang W, Ding X, Lu L.

Abstract: Inflammation is a key pathogenic factor in age-related macular degeneration (AMD). However, the clinical importance of combining anti-VEGF agents and topical NSAIDs to reduce inflammation remains unclear. In this study, we systematically reviewed clinical trials comparing combined treatment versus anti-VEGF alone in AMD patients. We quantified treatment effects via meta-analysis. The pooled weighted mean difference (WMD, -0.91, 95%CI: -1.39 to -0.42, P = 0.0003) demonstrates that combined treatment may reduce required anti-VEGF injection number, probably by means of decreasing central retina thickness (CRT) (WMD = -22.9, 95% CI: -41.20 to -4.59, P = 0.01). The best corrected visual acuity (BCVA) did not change significantly between these two groups (WMD = -0.01, 95%CI: -0.23 to 0.20, P = 0.90). Topical NSAIDs slightly increased the incidence of foreign body sensation (Odds Ratio [OR] = 2.63, 95%CI: 1.06 to 6.52, P = 0.76). Combining topical NSAIDs and anti-VEGF agents may provide a new strategy for AMD treatment.

PMID: 28985220


Efficacy and Safety of Ranibizumab With or Without Verteporfin Photodynamic Therapy for Polypoidal Choroidal Vasculopathy: A Randomized Clinical Trial.


IMPORTANCE: Polypoidal choroidal vasculopathy (PCV) is a common subtype of exudative age-related macular degeneration among Asian individuals. To our knowledge, there are no large randomized clinical trials to evaluate intravitreal ranibizumab, with and without verteporfin photodynamic therapy (vPDT), for the treatment of PCV.

OBJECTIVE: To compare the efficacy and safety of combination therapy of ranibizumab and vPDT with ranibizumab monotherapy in PCV.

DESIGN, SETTING, AND PARTICIPANTS: A double-masked, multicenter randomized clinical trial of 322 Asian participants with symptomatic macular PCV confirmed by the Central Reading Center using indocyanine green angiography was conducted between August 7, 2013, and March 2, 2017.

INTERVENTIONS: Participants were randomized 1:1 to ranibizumab, 0.5 mg, and vPDT (n = 168;
combination therapy group) or ranibizumab, 0.5 mg, and sham PDT (n = 154; monotherapy group). All participants received 3 consecutive monthly ranibizumab injections, followed by a pro re nata regimen. Participants also received vPDT/sham PDT on day 1, followed by a pro re nata regimen based on the presence of active polypoidal lesions.

MAIN OUTCOMES AND MEASURES: Step 1 assessed whether combination therapy was noninferior (5-letter margin) to monotherapy for change in best-corrected visual acuity from baseline and superior in complete polyp regression. If noninferiority was established, step 2 assessed whether combination therapy was superior to monotherapy measured by best-corrected visual acuity change at month 12.

RESULTS: Baseline demographics of the 322 participants were comparable between the treatment groups. Mean (SD) age of the patients was 68.1 (8.8) years, and overall, 69.9% of the patients were men. At baseline, the overall mean best-corrected visual acuity and mean central subfield thickness were 61.1 letters and 413.3 μm, respectively. At 12 months, mean improvement from baseline was 8.3 letters with combination therapy vs 5.1 letters with monotherapy (mean difference, 3.2 letters; 95% CI, 0.4-6.1), indicating that combination therapy met the predefined criterion for noninferiority as well as being superior to monotherapy (P = .01). Combination therapy was also superior to monotherapy in achieving complete polyp regression at month 12 (69.3% vs 34.7%; P < .001). Over 12 months, the combination therapy group received a median of 4.0 ranibizumab injections compared with 7.0 in the monotherapy group. Vitreous hemorrhage was the only ocular serious adverse event (combination therapy group, 1 [0.6%]; monotherapy group, 3 [2.0%]).

CONCLUSIONS AND RELEVANCE: After 12 months, combination therapy of ranibizumab plus vPDT was not only noninferior but also superior to ranibizumab monotherapy in best-corrected visual acuity and superior in complete polyp regression while requiring fewer injections. Combination therapy should be considered for eyes with PCV.

PMID: 28983556


Self-limited membranous nephropathy after intravitreal bevacizumab therapy for age-related macular degeneration.

Khneizer G, Al-Taee A, Bastani B.

BACKGROUND: Monoclonal antibodies targeting vascular endothelial growth factor (VEGF), such as bevacizumab, are administered intravitreally for the treatment of wet or exudative age-related macular degeneration (ARMD). Systemic use of bevacizumab has been linked to a wide range of renal adverse effects including proteinuria and hypertension.

CASE PRESENTATION: We present the case of a 77-year-old Caucasian male with a past medical history of hypertension, vitamin D deficiency and paroxysmal atrial fibrillation who presented to primary care clinic with a 2-week history of bilateral lower extremity edema, 2 months after completing four monthly intravitreal injections of bevacizumab for ARMD. Examination was remarkable for blood pressure of 187/91 mm Hg and severe bilateral lower extremity edema. Work up revealed unremarkable complete blood count (CBC), comprehensive metabolic panel (CMP), lipid panel, and echocardiography, except for 491 mg/dL albuminuria. Metoprolol and furosemide were added to hydrochlorothiazide and lisinopril. Work up by nephrology consult team five months later was notable for a urinalysis revealing 3 red blood cells/high power field (RBC/HPF), 24-hour urine protein of 8.6 g, and serum creatinine of 1.2 mg/dL. Viral hepatitis panel, total complement activity (CH50), C3, C4, anti-nuclear antibody (ANA), anti-neutrophil cytoplasmic antibody (ANCA), serum and urine protein electrophoresis were all unremarkable. Renal biopsy was consistent with membranous nephropathy. Age-appropriate cancer screening was negative. Random urine protein-to-creatinine ratio declined to 2 g/g and then to 0.56 g/g at 7 and 10 months follow up, respectively. Serum blood urea nitrogen (BUN) and creatinine remained normal throughout the course of illness and patient did not require any immnosuppressive treatment.
CONCLUSIONS: The wide range of nephrotoxicity after systemic bevacizumab has been well documented. Our case describes a self-limited biopsy-proven membranous nephropathy after intravitreal bevacizumab injections.

PMID: 28975092 PMCID: PMC5607973

Nanoscale. 2017 Oct 4. [Epub ahead of print]

Therapeutic effects of a novel siRNA-based anti-VEGF (siVEGF) nanoball for the treatment of choroidal neovascularization.


Abstract: Age-related macular degeneration (AMD) is the leading cause of blindness in developed countries and is characterized by the development of choroidal neovascularization (CNV). Therapies for AMD have focused on suppressing angiogenic factors, such as vascular endothelial growth factor (VEGF), mainly via conventional anti-VEGF antibody agents. However, additional efforts have been made to develop effective small-interfering RNA (siRNA)-based intracellular therapeutic agents. In this study, we have manufactured a novel siRNA-based anti-VEGF nanoball (siVEGF NB). The siVEGF NB was composed of a siRNA hydrogel with a core of anti-VEGF sequence siRNA coated with branched PEI (bPEI) and hyaluronic acid (HA) in order by applying an electrical force. The novel siVEGF NBs, which were employed in a laser-induced CNV mouse model, were optimized as a retinal and choroidal delivery system through the vitreous humor to the sub-retinal space via CD44 receptor endocytosis on the inner limiting membrane, and showed therapeutic effects via pathways bypassing the TLR3-induced siRNA-class effect. The therapeutic effects of siVEGF NBs lasted for 2 weeks after intravitreal injection showing high targeting efficiency to the sub-retinal space. Thus, the newly developed siVEGF NB may have great potential for the delivery of RNAi-based therapeutics for ocular diseases, including AMD.

PMID: 28976519


[Anti-VEGF therapy resistance in neovascular age-related macular degeneration]. [Article in Russian]

Budzinskaya MV, Plyukhova AA, Sorokin PA.

Abstract: With account to the increase in the elderly population in most of the developed countries, the WHO defines age-related macular degeneration (AMD) as one of the main causes of blindness in the world. A large percentage of disability is accounted for by exudative, or neovascular, form of AMD. Today, a total of 5 anti-VEGF drugs exist that are recommended for treatment of exudative AMD: pegaptanib, ranibizumab, bevacizumab, aflibercept, and conbercept. Despite significant progress in the treatment of neovascular AMD yielded by the introduction into clinical practice of anti-VEGF drugs, some patients report a lack (down to complete lack) of response with standard treatment patterns and even a decrease in treatment efficacy after repeated intravitreal injections.

PMID: 28980574

Other treatment & diagnosis


Comparison of Neovascular Lesion Area Measurements From Different Swept-Source OCT Angiographic Scan Patterns in Age-Related Macular Degeneration.

PURPOSE: We compared area measurements for the same neovascular lesions imaged using swept source optical coherence tomography angiography (SS-OCTA) and enlarging scan patterns.

METHODS: Patients with neovascular age-related macular degeneration were imaged using a 100-kHz SS-OCTA instrument (PLEX Elite 9000). The scanning protocols included the 3 × 3, 6 × 6, 9 × 9, and 12 × 12 mm fields of view. Two groups were studied. Group 1 included small lesions contained within the 3 × 3 mm scan, and Group 2 included larger lesions that were fully contained within the 6 × 6 mm scan.

RESULTS: A total of 30 eyes of 26 patients were enrolled in Group 1 and 30 eyes of 25 patients were enrolled in Group 2. In Group 1, the automated mean lesion area measurements were 1.11 (SD = 0.78), 1.14 (SD = 0.80), and 1.27 (SD = 0.82) mm² for the 3 × 3, 6 × 6, and 12 × 12 mm scans, respectively (ANOVA P < 0.001; post hoc comparisons, P = 0.184, 3 × 3 vs. 6 × 6 mm; P < 0.001 for the other two pairs). In Group 2, the automated mean lesion area measurements were 5.43 (SD = 2.56), 5.53 (SD = 2.48), and 5.49 (SD = 2.65) mm² for the 6 × 6, 9 × 9, and 12 × 12 mm scans, respectively (ANOVA P = 0.435; post-hoc comparisons, P = 0.062, 6 × 6 vs. 9 × 9 mm; P = 0.553, 6 × 6 vs. 12 × 12 mm; P = 0.654, 9 × 9 vs. 12 × 12 mm).

CONCLUSIONS: The similarity in lesion area measurements across different scan patterns suggests that SS-OCTA imaging can be used to follow quantitatively the enlargement of choroidal neovascularization as the disease progresses.

PMID: 28986595


Age-related macular degeneration: is polypoidal choroidal vasculopathy recognized and treated?


OBJECTIVE: To assess how polypoidal choroidal vasculopathy (PCV) is recognized and treated, and to assess whether treatment outcomes are different between Chinese and Caucasian Canadian patients with age-related macular degeneration (AMD).

DESIGN: Retrospective chart review.

PARTICIPANTS: 154 eyes from 135 Chinese patients and 2291 eyes from 1792 Caucasian patients who were newly diagnosed with either AMD or PCV and had more than 1 year of follow-up were included.

METHODS: All newly diagnosed AMD patients presenting to the Retina Service of 3 Toronto University Hospitals, between March 25, 2008, to September 30, 2014, were reviewed.

RESULTS: 10/154 eyes (6.5%) in Chinese Canadians and 16/2291 eyes (0.7%) in Caucasian Canadians were diagnosed as having PCV. Indocyanine green angiography (ICGA) was used to diagnose PCV in 20% of Chinese Canadians and 8.8% of Caucasian Canadians. Clinical practices with a larger percentage of Chinese patients were more likely to diagnose PCV in both Chinese (p = 0.004) and Caucasian patients (p = 0.03), were more likely to use photodynamic therapy (PDT) (p < 0.01), and had significantly greater central retinal thickness decrease (p < 0.001).

CONCLUSION: Our study has shown that PCV is under-recognized in a Canadian population, and ICGA is underutilized. In clinical practices with a greater portion of Chinese patients, PCV is more often recognized and PDT is used more liberally.

PMID: 28985807
Signal reduction in choriocapillaris and segmentation errors in spectral domain OCT angiography caused by soft drusen.

Alten F, Lauermann JL, Clemens CR, Heiduschka P, Eter N.

PURPOSE: To analyze signal reduction in choriocapillaris (CC) and segmentation errors in spectral domain optical coherence tomography angiography (OCT-A) caused by soft drusen due to age-related macular degeneration (AMD).

METHODS: Twenty-four eyes of 24 patients underwent multimodal retinal imaging including central 3 × 3mm2 OCT-A (AngioVue, Optovue). Three drusen per study eye were randomly chosen and evaluated regarding drusen height, diameter, and accuracy of OCT-A layer segmentation in lesion proximity. Structural en-face OCT CC images were graded qualitatively and quantitatively regarding signal loss underneath the individual drusen area. Those drusen that showed no distinct signal loss in structural en-face OCT CC images were further evaluated in OCT-A. CC decorrelation signal index was measured within a 30-μm OCT-A CC slab in the exact area of drusen affection. Data were compared to healthy age-matched control subjects. Accuracy of layer segmentation, OCT CC data, and OCT-A CC data were correlated to morphological drusen parameters.

RESULTS: Mean drusen height and diameter were 91.57 ± 19.5μm and 315.17 ± 116.7μm. OCT-A layer segmentation of the inner plexiform layer (IPL) was disturbed by more than 50 μm in proximity to 26 drusen (36.1%). In these patients, drusen height was significantly higher compared to those with accurate IPL segmentation (p = 0.0126). Sixty-six out of 72 drusen (91.7%) caused a distinct signal loss in the structural en-face OCT CC image. Drusen height and drusen diameter were significantly higher in this group compared to the six drusen with a sufficient signal (p = 0.0276, p = 0.0025). CC decorrelation signal index measured in the area of these six drusen without OCT signal loss (8.3%) was reduced compared to age-matched healthy controls (73.6 vs. 100.1; p = 0.001).

CONCLUSIONS: Signal attenuation in CC slabs and segmentation errors of the IPL depend on drusen morphology. Both are frequent artifacts in OCT-A imaging in patients with soft drusen and must be considered during image analysis.

PMID: 28983695
hyperreflective areas in the EZ band correlated topographically with hyporeflective foci at the level of the RPE.

CONCLUSIONS: The hyperreflective lesions corresponding to RPD in SD-OCT scans are likely indicative of degenerating photoreceptor cells. The darkened foci at positions of RPD in NIR-AF and en face OCT images indicate changes in the RPE monolayer with the reduced NIR-AF and en face OCT signal suggesting a reduction in melanin that could be accounted for by RPE thinning.

PMID: 28973322 PMCID: PMC5624777


Automated detection of foveal center in SD-OCT images using the saliency of retinal thickness maps.

Niu S, Chen Q, de Sisternes L, Leng T, Rubin DL.

PURPOSE: To develop an automated method based on saliency map of the retinal thickness map to determine foveal center in spectral-domain optical coherence tomography (SD-OCT) images.

METHODS: This paper proposes an automatic method for the detection of the foveal center in SD-OCT images. Initially, a retinal thickness map is generated by considering the axial distance between the internal limiting membrane (ILM) and the Bruch's membrane (BM). Both the ILM and BM boundaries are automatically segmented by a known retinal segmentation technique. The macular foveal region is identified as a salient feature in the retinal thickness map, and segmented by the saliency detection method based on a human vision attention model. Finally, the foveal center is identified by searching for the lowest point from the determined macular fovea region.

RESULTS: Experimental results in 39 scans from 35 healthy eyes and 58 scans from 29 eyes diagnosed with several stages of age-related macular degeneration (AMD), from mild or intermediate stages to severe dry or wet stages, demonstrated that the proposed method achieves good performance. The mean radial distance error of the automatically detected foveal center locations when compared to consensus manual determination established by repeated sessions from two expert readers was 52 ± 56 μm for the normal eyes and 73 ± 63 μm for AMD eyes.

CONCLUSIONS: The proposed algorithm was more effective for detecting the foveal center automatically in SD-OCT images than the state-of-art methods. This article is protected by copyright. All rights reserved.

PMID: 28976639

Ophthalmologe. 2017 Oct 4. [Epub ahead of print]

[Statement from the BVA, the DOG and the RG on laser treatment of drusen in age-related macular degeneration (AMD) : August 2017]. [Article in German]

Berufsverband der Augenärzte Deutschlands e.V.; Deutsche Ophthalmologische Gesellschaft; Retinologische Gesellschaft e. V..

PMID: 28980062
Pathogenesis


Therapeutic Effects of PPARα Agonist on Ocular Neovascularization in Models Recapitulating Neovascular Age-Related Macular Degeneration.


PURPOSE: This study was designed to evaluate effects of fenofibric acid (Feno-FA), a peroxisome proliferator-activated receptor-alpha (PPARα) agonist, on ocular neovascularization (NV) in models recapitulating neovascular age-related macular degeneration (AMD), and to explore whether the effects are PPARα dependent.

METHODS: Laser-induced choroidal NV (CNV) in rats and very low-density lipoprotein receptor knockout (Vldlr-/-) mice received daily intraperitoneal injections of Feno-FA or vehicle. Vascular leakage was examined by fundus fluorescein angiography and permeability assay using Evans blue as tracer. In CNV rats, severity of CNV was evaluated by CNV areas and CNV volume. In Vldlr-/- mice, subretinal NV (SRNV) and intraretinal NV (IRNV) were quantified in choroid flat mount and retina flat mount, respectively. Inflammatory factors were measured using Western blotting and retinal leukostasis assay. Further, Ppara-/- mice and age-matched wild-type (WT) mice were used for laser-induced CNV and treated with Feno-FA to explore the underlying mechanism.

RESULTS: Feno-FA significantly reduced vascular leakage in CNV rats and Vldlr-/- mice, reduced CNV volume in laser-induced CNV rats, and suppressed SRNV and IRNV in Vldlr-/- mice. In addition, Feno-FA downregulated the expression of inflammatory factors, including VEGF, TNFα, and intercellular cell adhesion molecule-1 (ICAM-1), in the eyecups of CNV rats and decreased adherent retinal leukocytes in Vldlr-/- mice. Furthermore, Ppara-/- mice developed more severe CNV compared with WT mice, and PPARα knockout abolished the beneficial effects of Feno-FA on CNV.

CONCLUSIONS: Feno-FA has therapeutic effects on ocular NV in models recapitulating neovascular AMD through a PPARα-dependent mechanism.

PMID: 28980001


Quantitative phosphoproteomics reveals involvement of multiple signaling pathways in early phagocytosis by the retinal pigmented epithelium.

Chiang CK, Tworak A, Kevany BM, Xu B, Mayne J, Ning Z, Figeys D, Palczewski K.

Abstract: One of the major biological functions of the retinal pigmented epithelium (RPE) is the clearance of shed photoreceptor outer segments (POS) through a multistep process resembling phagocytosis. RPE phagocytosis helps maintain the viability of photoreceptors that otherwise could succumb to the high metabolic flux and photo-oxidative stress associated with visual processing. The regulatory mechanisms underlying phagocytosis in the RPE are not fully understood, although dysfunction of this process contributes to the pathogenesis of multiple human retinal degenerative disorders, including age-related macular degeneration. Here, we present an integrated transcriptomic, proteomic, and phosphoproteomic analysis of phagocytosing RPE cells, utilizing three different experimental models: human-derived RPE-like cell line, ARPE-19, cultured murine primary RPE cells, and RPE samples from live mice. Our combined results indicated that early stages of phagocytosis in the RPE are mainly characterized by pronounced changes in the protein phosphorylation level. Global phosphoprotein enrichment analysis revealed involvement of PI3K/Akt, mechanistic target of rapamycin (mTOR), and MEK/ERK pathways in the regulation of RPE phagocytosis, confirmed by immunoblot analyses and in vitro phagocytosis assays. Most strikingly, phagocytosis of POS by cultured RPE cells was almost completely blocked by pharmacological inhibition of phosphorylation of Akt. Our findings, along with those of previous studies, indicate that these
phosphorylation events allow the RPE to integrate multiple signals instigated by shed POS at different stages of the phagocytic process.

PMID: 28978645

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Long-term photoreceptor rescue in two rodent models of retinitis pigmentosa by adeno-associated virus delivery of Stanniocalcin-1.

Roddy GW, Yasumura D, Matthes MT, Alavi MV, Boye SL, Rosa RH Jr, Fautsch MP, Hauswirth WW, LaVail MM.

Abstract: Retinal degenerations, including age-related macular degeneration and the retinitis pigmentosa family of diseases, are among the leading causes of legal blindness in the United States. We previously found that Stanniocalcin-1 (STC-1) reduced photoreceptor loss in the S334ter-3 and Royal College of Surgeons rat models of retinal degeneration. The results were attributed in part to a reduction in oxidative stress. Herein, we tested the hypothesis that long-term delivery of STC-1 would provide therapeutic rescue in more chronic models of retinal degeneration. To achieve sustained delivery, we produced an adeno-associated virus construct (AAV) to express STC-1 (AAV-STC-1) under the control of a retinal ganglion cell targeting promoter human synapsin 1 (hSYN1). AAV-STC-1 was injected intravitreally into the P23H-1 and S334ter-4 rhodopsin transgenic rats at postnatal day 10. Tissues were collected at postnatal day 120 for confirmation of STC-1 overexpression and histologic and molecular analysis. Electroretinography (ERG) was performed in a cohort of animals at that time. Overexpression of STC-1 resulted in a significant preservation of photoreceptors as assessed by outer nuclear thickness in the P23H-1 (P < 0.05) and the S334ter-4 (P < 0.005) models compared to controls. Additionally, retinal function was significantly improved in the P23H-1 model with overexpressed STC-1 as assessed by ERG analysis (scotopic b-wave P < 0.005 and photopic b-wave P < 0.05). Microarray analysis identified common downstream gene expression changes that occurred in both models. Genes of interest based on their function were selected for validation by quantitative real time PCR and were significantly increased in the S334ter-4 model.

PMID: 28974356


Topical Ocular Delivery of TGF-β1 to the Back of the Eye: Implications in Age-Related Neurodegenerative Diseases.


Abstract: Dysregulation of the transforming growth factor-β1 (TGF-β1)/selected small mother against decapentaplegic (SMAD) pathway can be implicated in development of age-related macular degeneration (AMD), and the delivery of TGF-β1 could be beneficial for AMD. We developed a new ophthalmic formulation of TGF-β1 assessing the ocular pharmacokinetic profile of TGF-β1 in the rabbit eye. Small unilamellar vesicles (SUV) loaded with TGF-β1 were complemented with Annexin V and Ca2+, and the vitreous bioavailability of TGF-β1 was assessed after topical ocular administration by a commercial ELISA kit. We detected high levels of TGF-β1 (Cmax 114.7 ± 12.40 pg/mL) in the vitreous after 60 min (Tmax) from the topical application of the liposomal suspension. Ocular tolerability was also assessed by a modified Draize's test. The new formulation was well tolerated. In conclusion, we demonstrated that the novel formulation was able to deliver remarkable levels of TGF-β1 into the back of the eye after topical administration. Indeed, this TGF-β1 delivery system may be useful in clinical practice to manage ophthalmic conditions such as age-related macular degeneration, skipping invasive intraocular injections.

PMID: 28973964
Genetics & gene therapy


Genetics of age-related macular degeneration (AMD).


PMID: 28977452

Diet, lifestyle & low vision


Nutritional and smoking advice recalled by patients attending a UK age-related macular degeneration clinic.

Bott D, Huntjens B, Binns A.

BACKGROUND: Age-related macular degeneration (AMD) is responsible for half of registered visual impairment in the UK. The Royal College of Ophthalmologists recommends providing guidance to people with AMD regarding smoking, diet, and nutritional supplements. The aim of this study was to investigate lifestyle advice recalled by patients with neovascular AMD (nAMD).

METHODS: The study took place at a UK hospital outpatients’ clinic. Eligible patients with unilateral nAMD were presented with a survey about lifestyle advice provision.

RESULTS: Of 248 respondents, only 39.9% remembered receiving advice regarding diet at the hospital. Only 24.2% of respondents recalled receiving advice regarding nutritional supplements, and only 19.8% of respondents started taking daily supplements as a result of their AMD. The most prevalent reason for not taking supplements amongst those advised to do so was lack of understanding of how it would help their eyes. Nearly 13% of the sample reported currently smoking, 53.1% of which reported that they were advised to stop smoking when diagnosed with AMD.

CONCLUSION: The findings suggest that it would be beneficial to review the provision of lifestyle advice to patients attending AMD outpatients' clinics, and to consider whether advice is being provided in an optimal format for later recall.

PMID: 28977430


Resveratrol Ameliorates Retinal Ischemia/Reperfusion Injury in C57BL/6J Mice via Downregulation of Caspase-3.

Seong H, Ryu J, Yoo WS, Kim SJ, Han YS, Park JM, Kang SS, Seo SW.

PURPOSE: Ischemia/reperfusion (I/R) injury induces apoptosis in retinal ganglion cells (RGCs). Resveratrol (Res) is a potent natural antioxidant with beneficial effects in many ocular diseases, such as age-related macular degeneration, diabetic retinopathy, and glaucoma. Because caspase-3 expression is highly correlated with activation of the apoptotic pathway, the present study aimed to determine whether Res regulates the expression of caspase-3 using an I/R retinal injury mouse model.

METHODS: Male C57BL/6J mice were injected with Res for 2 consecutive days before I/R retinal injury. I/R retinal injury was induced by increasing the intraocular pressure for 1 h. Res was then injected for 3 consecutive days. Changes in retinal morphology were monitored for 3 days after injury by histochemistry.
using hematoxylin and eosin staining. mRNAs and proteins were extracted 2 days after injury. The expression levels of caspase-8 and caspase-3 mRNA and protein were determined using reverse-transcriptase polymerase chain reaction (RT-PCR) and western blot analyses.

RESULTS: I/R injury induced declines in retinal thickness and number of RGCs during 5 days after injury. Caspase-8 and caspase-3 mRNA and protein activation increased. Res treatment reduced the significant loss of retinal morphology and downregulated the expression of mRNA and activation of caspase-8 and caspase-3 protein.

CONCLUSIONS: The observed changes in retinal morphology suggest that I/R injury promotes retinal degeneration. Increased expression of caspase-8 and caspase-3 mRNA indicates apoptosis activation. Res, however, suppresses apoptosis via downregulation of caspase-8 and caspase-3 expression.

PMID: 28985092

Eur J Ophthalmol. 2017 Oct 5:0. [Epub ahead of print]

Consecutive case series of 244 age-related macular degeneration patients undergoing implantation with an extended macular vision IOL.

Qureshi MA, Robbie SJ, Hengerer FH, Auffarth GU, Conrad-Hengerer I, Artal P.

PURPOSE: To determine safety and visual outcomes in eyes with age-related macular degeneration (AMD) implanted with a novel intraocular lens (IOL) that delivers an optimized retinal image to all macular areas within 10 degrees of retinal eccentricity.

METHODS: This was a consecutive case series of 244 eyes with dry/stable wet AMD and logMAR visual acuity ≥0.3 implanted with iolAMD Eyemax monoTM (London Eye Hospital Pharma), a single-piece, injectable, hydrophobic acrylic IOL sited in the capsular bag. Primary outcome was safety. Secondary outcomes were changes in corrected distance visual acuity (CDVA) and corrected near visual acuity (CNVA) (logMAR).

RESULTS: Mean age at surgery was 80 years. Mean duration of follow-up was 3 months (range 1-16 months). No eyes had worsening of CDVA. Frequency of perioperative complications was equivalent to standard IOL implantation. Postoperative refractive outcomes were within ±1 D of the target refraction in 88% of cases. Mean preoperative CDVA improved from 1.06 to 0.71 postoperatively (mean of differences -0.35; 95% confidence interval [CI] -0.3886 to -0.3223; p<0.0001), equating to an approximate Early Treatment Diabetic Retinopathy Study gain of 18 letters. Mean preoperative CNVA (N-point; logMAR conversion) improved from 1.36 to 0.88 postoperatively (mean of differences -0.48; 95% CI -0.53 to -0.44; p<0.0001).

CONCLUSIONS: This novel IOL appears safe in the short to medium term. Improvements in postoperative CDVA and CNVA exceed those observed with standard implants.

PMID: 28983894

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