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MD Research News

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Drug treatment

Ophthalmologica. 2014 Aug 29. [Epub ahead of print]

Switch from Intravitreal Ranibizumab to Bevacizumab for the Treatment of Neovascular Age-Related Macular Degeneration: Clinical Comparison.

Pinheiro-Costa J, Freitas-da-Costa P, Falcão MS, Brandão EM, Falcão-Reis F, Carneiro AM.

Objective: To compare outcomes after switching from intravitreal ranibizumab to bevacizumab in neovascular age-related macular degeneration (AMD).

Methods: A retrospective review of 110 eyes treated in a 1+PRN (pro re nata) clinical setting with ranibizumab that were switched to bevacizumab. Patients analyzed had at least 3 ranibizumab injections followed by at least 3 bevacizumab injections. Changes in best-corrected visual acuity (BCVA), retinal thickness and frequency of injections were compared.

Results: The mean duration of ranibizumab treatment was 18.1 months, followed by 12.2 months of bevacizumab. Mean injection rates per month were similar (0.54 and 0.56 respectively, $p = 0.230$). There were no significant differences between BCVA at baseline and at the time of the switch (52.4 and 54.8 letters, $p = 0.059$). After the switch, there was a statistically significant decrease in BCVA to 51.7 letters ($p < 0.001$).

Conclusion: Switching patients to bevacizumab may have a minor negative effect on the initial gain obtained with ranibizumab; however the degenerative history of wet AMD could explain this small variation in visual acuity.

PMID: 25196907 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2014 Sep 10. [Epub ahead of print]

Intravitreal Ranibizumab for neovascular Age-related macular degeneration in clinical practice: five-year treatment outcomes.

Zhu M, Chew JK, Broadhead GK, Luo K, Joachim N, Hong T, Syed A, Chang AA.

BACKGROUND: Intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents are the established standard of care for neovascular age-related macular degeneration (nAMD). However, data on long-term outcomes of this therapy are limited. The purpose of this study was to assess the visual and anatomical

outcomes and safety profile of intravitreal ranibizumab in treating nAMD over a period of five years.

METHODS: 208 patients (208 eyes) were included in this retrospective case series study. Intervention was an "as-needed" treatment model. Visual acuity (VA), central macular thickness (CMT), ophthalmic examination, and adverse events (AEs) were assessed in each visit. Snellen VA was converted to Early Treatment Diabetic Retinopathy Study letters for analysis.

RESULTS: The average VA improved by 1.9 letters after one year ($p = 0.017$), and decreased by 2.4 letters over five years of treatment ($p = 0.043$). At the end of year five, 11.1 % of patients (23/208) had improved VA by more than 15 letters and 68.8 % (143/208) had VA improvement or loss less than or equal to 15 letters, while 20.2 % of patients (42/208) had a loss of more than 15 letters. Patients with VA of less than 35 letters at baseline showed significant VA improvement after five years of treatment. There was a positive relationship between injection numbers and VA improvement over the five-year period, after adjusting for age and baseline VA ($p < 0.0005$). Mean CMT decreased by 28.3 μm ($p < 0.0005$) over five years. Ocular AEs, serious adverse events (SAEs), and systemic SAEs occurred in 4.6 %, 0.48 %, and 2 % of patients, respectively, during the follow-up period.

CONCLUSIONS: The use of intravitreal ranibizumab in an as-needed treatment regimen over a five-year period was effective in maintaining vision in patients with nAMD and in reducing macular thickness, with a relatively low rate of adverse and serious adverse events.

PMID: 25205618 [PubMed - as supplied by publisher]

J Ocul Pharmacol Ther. 2014 Sep 12. [Epub ahead of print]

Success of Ranibizumab in Central Serous Chorioretinopathy Resistant to Bevacizumab.

Altun A, Kurna SA, Olcaysu OO, Sengor T, Aki SF, Atakan TG.

Purpose: To present effectiveness of intravitreal ranibizumab (IVR) injection for central serous chorioretinopathy (CSC), resistant to intravitreal bevacizumab (IVB) injection.

Methods: Files of the patients who had the diagnosis of CSC between 2005 and 2013 were reviewed retrospectively. Eighty-five eyes of 81 patients' files have been investigated. Ten eyes of 10 patients that were resistant to IVB, with no history of photodynamic therapy, were included in to this study. Demographic details, best-corrected visual acuity (BCVA), and central macular thickness (CMT) were studied to analyze the effectiveness of IVR.

Results: The mean age of the patients was 38.8 years (SD=4.7 years). The mean follow-up time after first IVR injection was 7.9 months (SD=1.5 months). The mean number of IVB and IVR injections was 2.0 (SD=0.7) and 1.3 (SD=0.4), respectively. The mean CMT before IVR injection was 392.4 μm (SD=66.3) and decreased to 194.1 μm (SD=9.3, P<0.001) at the last visit. The mean BCVA before IVR injection was 0.50logMAR (SD=0.23) and improved to 0.05logMAR (SD=0.06, P<0.001) at the last visit. In all cases after IVR injection, the subretinal fluid almost resolved completely, and leakage disappeared in fundus fluorescein angiography.

Conclusion: Ranibizumab might be a promising option for the patients with CSC, resistant to bevacizumab in acute or early chronic stage.

PMID: 25216333 [PubMed - as supplied by publisher]

Curr Opin Ophthalmol. 2014 Sep 10. [Epub ahead of print]

Diabetic macular edema: changing treatment paradigms.

Arevalo JF.

PURPOSE OF REVIEW: To review the current management and recent changes in treatment paradigm for diabetic macular edema (DME).

RECENT FINDINGS: During the review period (1 year), several prospective studies analyzed the beneficial effect of anti-vascular endothelial growth factor agents in the management of DME. An exploratory analysis concluded that intravitreal ranibizumab appears to be associated with a reduced risk of diabetic retinopathy worsening. A randomized, controlled, multicenter, double-masked, parallel-group, 12-month trial to evaluate a dexamethasone intravitreal implant (DEX implant) combined with laser photocoagulation compared with laser alone for treatment of DME concluded that there was no significant between-group difference at month 12. A multicenter, prospective, observational study found that in eyes with diabetic retinopathy without concurrent central-involved DME, presence of noncentral-involved DME immediately prior to cataract surgery or history of DME treatment may increase the risk of developing central-involved macular edema after cataract extraction. Another randomized trial to evaluate whether intravitreal ranibizumab injection at cataract surgery prevents postoperative DME concluded that intravitreal ranibizumab injection at cataract surgery may prevent the postoperative worsening of macular edema.

SUMMARY: The results of clinical trials have shown the superiority of some of these anti-vascular endothelial growth factor agents to laser therapy. However, with the availability of several of these newer agents, it may be difficult to individualize treatment options, especially if DME patients respond differently to various therapies.

PMID: 25211039 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2014 Aug 26;8:1611-21.

Clinical utilization of anti-vascular endothelial growth-factor agents and patient monitoring in retinal vein occlusion and diabetic macular edema.

Kiss S, Liu Y, Brown J, Holekamp NM, Almony A, Campbell J, Kowalski JW.

PURPOSE: To examine the utilization of bevacizumab and ranibizumab and disease monitoring in patients with branch or central retinal vein occlusion (BRVO/CRVO) or diabetic macular edema (DME) in clinical practice.

PATIENTS AND METHODS: This retrospective claims analysis included newly diagnosed patients with one or more bevacizumab or ranibizumab injections. Bevacizumab or ranibizumab utilization was assessed by year of first injection: 2008-2010 cohorts (12-month follow-up), January to June 2011 cohort (6-month follow-up). The main outcome measures were mean annual numbers of injections, ophthalmologist visits and optical coherence tomography examinations, and proportion of patients with additional laser or intravitreal triamcinolone (IVTA) use.

RESULTS: A total of 885 BRVO, 611 CRVO, and 2,733 DME patients treated with bevacizumab were included, with too few ranibizumab-treated patients for meaningful analysis. Across the 2008, 2009, and 2010 cohorts, mean annual numbers of bevacizumab injections increased, but remained low (BRVO 2.5, 3.1, 3.3; CRVO 3.1, 3.1, 3.5; and DME 2.2, 2.5, 3.6, respectively); mean ophthalmologist visits ranged between 4.4 and 6.5, and mean optical coherence tomography examinations ranged between 3.1 and 3.9 across all conditions. A total of 42.0% of BRVO, 16.5% of CRVO, and 57.7% of DME patients received additional laser or IVTA therapy. The number of bevacizumab injections was positively associated with laser use in BRVO (3.3 versus 2.9, $P<0.03$), and with laser or IVTA use in DME (laser, 3.3 versus 2.7, $P<0.03$; IVTA, 3.3 versus 3.0, $P<0.05$).

CONCLUSION: During the study period (2008-2011), bevacizumab was the main anti-VEGF therapy used in clinical practice for BRVO, CRVO, and DME. Patients treated with bevacizumab were monitored less

frequently and received fewer injections than patients in major clinical trials of ranibizumab.

PMID: 25210429 [PubMed] PMCID: PMC4155807

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

REPAIR MECHANISM OF RETINAL PIGMENT EPITHELIAL TEARS IN AGE-RELATED MACULAR DEGENERATION.

Mukai R, Sato T, Kishi S.

PURPOSE: To investigate repair mechanisms of retinal pigment epithelial (RPE) tears in age-related macular degeneration.

METHODS: The authors retrospectively studied 10 eyes with age-related macular degeneration that developed RPE tears during follow-up or after treatment with an anti-vascular endothelial growth factor drug or photodynamic therapy combined with ranibizumab. After development of the RPE tears, all follow-ups exceeded 13 months. Spectral domain or swept-source optical coherence tomography have been used to examine consecutive retinal changes where the RPE tears developed and attempted to determine the repair mechanisms.

RESULTS: Retinal pigment epithelial tears developed during the natural course (n = 4) after ranibizumab treatment (n = 2) and after photodynamic therapy and ranibizumab (n = 4). Subretinal fluid persisted for more than 6 months after the RPE tears developed (n = 4), with the area where the RPE was lost found to be covered with thickened proliferative tissue. In 6 eyes where the subretinal fluid was absorbed within 2 months, optical coherence tomography showed the outer retina appeared to be directly attached to Bruch membrane, and there was attenuation of the normal hyperreflective band attributable to normal RPE during follow-up.

CONCLUSION: Results suggest that two repair processes may be present in the area where RPE tears developed. Persistent subretinal fluid may lead to repair with thick proliferative tissue, while the outer retina appears to attach to Bruch membrane when there is early subretinal fluid resolution after RPE tear development.

PMID: 25207945 [PubMed - as supplied by publisher]

BMC Res Notes. 2014 Sep 8;7(1):617. [Epub ahead of print]

Gene profiling of human VEGF signaling pathways in human endothelial and retinal pigment epithelial cells after anti VEGF treatment.

Golan S, Entin-Meer M, Semo Y, Maysel-Auslender S, Mezad-Koursh D, Keren G, Loewenstein A, Barak A.

BACKGROUND: Ranibizumab (Lucentis(R)) is a Fab-antibody fragment developed from Bevacizumab, a full-length anti-VEGF antibody. Both compounds are used for treating age-related macular degeneration (AMD). The influence of bevacizumab and ranibizumab on genes involved in signal transduction and cell signaling downstream of VEGF were compared in order to detect possible differences in their mode of action, which are not related to their Fab-antibody fragments.

METHODS: Human umbilical vein cell lines (EA.hy926) and retinal pigment epithelial cells (ARP-19) were exposed to oxidative stress. The cells were treated with therapeutic concentrations of bevacizumab (0.25 mg/mL) and ranibizumab (125 mg/mL) for 24 hours prior to all experiments, and their effects on gene expressions were determined by RT- PCR.

RESULTS: After exposure to bevacizumab, more genes in the endothelial cells were up-regulated (KDR, NFATc2) and down-regulated (Pla2g12a, Rac2, HgdC, PRKCG) compared to non-treated controls. After exposure to ranibizumab, fewer genes were up-regulated (PTGS2) and down-regulated (NOS3) compared to controls. In comparison between drugs, more genes were up-regulated (NFATc2 and KDR) and more were down-regulated (Pla2g12a, Pla2g1b, Ppp3r2, Rac2) by bevacizumab than by ranibizumab. In RPE cells, NOS3 and PGF were up-regulated and Pla2g12b was down-regulated after exposure to ranibizumab, while PIK3CG was up-regulated and FIGF was down-regulated after exposure to bevacizumab, but the differences in gene expression were minor between drugs (PIK3CGand PGF were down-regulated more by ranibizumab than by bevacizumab).

CONCLUSIONS: The different gene expressions after exposure to ranibizumab and bevacizumab in endothelial and RPE cells may indicate a somewhat different biological activity of the two compounds.

PMID: 25201034 [PubMed - as supplied by publisher]

Med Arh. 2014;68(3):204-8.

Therapeutic modalities of exudative age-related macular degeneration.

Mavija M, Alimanovic E, Jaksic V, Kasumovic SS, Cekic S, Stamenkovic M.

INTRODUCTION: Age-related macular degeneration (AMD) is a leading cause of irreversible serious vision damage in persons over 50 years of age. In treating AMD many medicaments are applied such as inhibitors of vascular endothelial growth factor (VEGF), have been very carefully included over the last few years after a series of study research.

AIMS: To analyze the past methods of treatment, discuss emerging therapies which could advance the treatment of exudative AMD. The past anti-VEGF therapies require frequent repetitions of administration, with uncertain visual acuity recovery, as not all patients react to anti-VEGF therapy. Consequently, there is a need to find out additional therapies which could improve the treatment of exudative AMD. The real aim in the treating of AMD is to prevent CNV development.

METHODS: A survey of the current clinical research and results in the field of the present and future treatments of exudative AMD.

RESULTS: There are many areas of research into new methods of the exudative AMD treatment.

CONCLUSION: The future therapies for exudative AMD treatment have a potential not only to reduce the frequency of administration and follow-up visits, but also to improve effects of treatment by targeting additional ways of CNV development, increasing the aptitude of target binding and extending durability of treatment.

PMID: 25195354 [PubMed - in process]

JAMA. 2014 Aug 27;312(8):847-8.

Cost-related motivations for research--reply.

Nayak RK, Miller FG.

Comment on

Cost-related motivations for conducting research: participants should be informed. [JAMA. 2014]

Cost-related motivations for research. [JAMA. 2014]

PMID: 25157736 [PubMed - indexed for MEDLINE]

JAMA. 2014 Aug 27;312(8):847.

Cost-related motivations for research.

Martin DF, Fine SL, Maguire MG.

Comment in

Cost-related motivations for research--reply. [JAMA. 2014]

Comment on

Cost-related motivations for conducting research: participants should be informed. [JAMA. 2014]

PMID: 25157735 [PubMed - indexed for MEDLINE]

Other treatment & diagnosis

Clin Ophthalmol. 2014 Aug 30;8:1661-70.

Epimacular brachytherapy for wet AMD: current perspectives.

Casaroli-Marano RP, Alforja S, Giralt J, Farah ME.

Abstract: Age-related macular degeneration (AMD) is considered the most common cause of blindness in the over-60 age group in developed countries. There are basically two forms of presentation: geographic (dry or atrophic) and wet (neovascular or exudative). Geographic atrophy accounts for approximately 85%-90% of ophthalmic frames and leads to a progressive degeneration of the retinal pigment epithelium and the photoreceptors. Wet AMD causes the highest percentage of central vision loss secondary to disease. This neovascular form involves an angiogenic process in which newly formed choroidal vessels invade the macular area. Today, intravitreal anti-angiogenic drugs attempt to block the angiogenic events and represent a major advance in the treatment of wet AMD. Currently, combination therapy for wet AMD includes different forms of radiation delivery. Epimacular brachytherapy (EMBT) seems to be a useful approach to be associated with current anti-vascular endothelial growth factor agents, presenting an acceptable efficacy and safety profile. However, at the present stage of research, the results of the clinical trials carried out to date are insufficient to justify extending routine use of EMBT for the treatment of wet AMD.

PMID: 25210436 [PubMed] PMCID: PMC4155998

Ophthalmology. 2014 Sep 7. [Epub ahead of print]

Visual Consequences of Refractive Errors in the General Population.

Verhoeven VJ, Wong KT, Buitendijk GH, Hofman A, Vingerling JR, Klaver CC.

OBJECTIVE: To study the frequency and causes of visual impairment in relation to refractive error.

DESIGN: Population-based cohort study.

PARTICIPANTS: A total of 6597 participants from Rotterdam Study I (baseline and 4 follow-up examinations) and 2579 participants from Rotterdam Study II (baseline and 2 follow-up examinations), all

55 years or older, were included.

METHODS: Participants underwent an extensive ophthalmic examination, including best-corrected visual acuity and objective refraction, fundus photography, visual field perimetry, and optical coherence tomography imaging of macula and optic disc. We calculated cumulative risks and odds ratios of visual impairment for various refractive error categories and determined causes by using all screening information as well as medical records.

MAIN OUTCOME MEASURES: Unilateral and bilateral low vision (World Health Organization [WHO] criteria, VA <0.3 and VA ≥0.05; United States (US) criteria, VA <0.5 and VA ≥0.1) and blindness (WHO criteria, VA <0.05; US criteria, VA<0.1).

RESULTS: Cumulative risks of visual impairment ranged from virtually 0 in all refractive error categories at 55 years of age to 9.5% (standard error, 0.01) for emmetropia and 15.3% (standard error, 0.06) for high hyperopia to 33.7% (standard error, 0.08) for high myopia at 85 years of age. The major causes of visual impairment in highly hyperopic persons were age-related macular degeneration (AMD), cataract, and combined causes (each 25%); in highly myopic persons, the major cause was myopic macular degeneration (38.9%). The major causes of visual impairment for the other refractive error categories were AMD and cataract. Compared with those with emmetropia, those with high myopia had a significantly increased lifetime risk of visual impairment; those with -6 diopters (D) or less and -10 D or more had an odds ratio (OR) risk of 3.4 (95% confidence interval [CI], 1.4-8.2) of visual impairment; those with less than -10 D had an OR of 22.0 (95% CI, 9.2-52.6).

CONCLUSIONS: Of all refractive errors, high myopia has the most severe visual consequences. Irreversible macular pathologic features are the most common cause of visual impairment in this group.

PMID: 25208857 [PubMed - as supplied by publisher]

Ophthalmology. 2014 Aug 29. [Epub ahead of print]

Gaps in Receipt of Regular Eye Examinations among Medicare Beneficiaries Diagnosed with Diabetes or Chronic Eye Diseases.

Sloan FA, Yashkin AP, Chen Y.

OBJECTIVE: To examine a wide range of factors associated with regular eye examination receipt among elderly individuals diagnosed with glaucoma, age-related macular degeneration, or diabetes mellitus (DM).

DESIGN: Retrospective analysis of Medicare claims linked to survey data from the Health and Retirement Study (HRS).

PARTICIPANTS: The sample consisted of 2151 Medicare beneficiaries who responded to the HRS.

METHODS: Medicare beneficiaries with ≥1 of the 3 study diagnoses were identified by diagnosis codes and merged with survey information. The same individuals were followed for 5 years divided into four 15-month periods. Predictors of the number of periods with an eye examination evaluated were beneficiary demographic characteristics, income, health, cognitive and physical function, health behaviors, subjective beliefs about longevity, the length of the individual's financial planning horizon, supplemental health insurance coverage, eye disease diagnoses, and low vision/blindness at baseline. We performed logit analysis of the number of 15-month periods in which beneficiaries received an eye examination.

MAIN OUTCOME MEASURES: The primary outcome measure was the number of 15-month periods with an eye examination.

RESULTS: One third of beneficiaries with the study's chronic diseases saw an eye care provider in all 4 follow-up periods despite having Medicare. One quarter only obtained an eye examination at most during 1

of the four 15-month follow-up periods. Among the 3 groups of patients studied, utilization was particularly low for persons with diagnosed DM and no eye complications. Age, marriage, education, and a higher score on the Charlson index were associated with more periods with an eye examination. Male gender, being limited in instrumental activities of daily living at baseline, distance to the nearest ophthalmologist, and low cognitive function were associated with a reduction in frequency of eye examinations.

CONCLUSIONS: Rates of eye examinations for elderly persons with DM or frequently occurring eye diseases, especially for DM, remain far below recommended levels in a nationally representative sample of persons with health insurance coverage. Several factors, including limited physical and cognitive function and greater distance to an ophthalmologist, but not health insurance coverage, account for variation in regular use.

PMID: 25208856 [PubMed - as supplied by publisher]

Ophthalmology. 2014 Sep 4. [Epub ahead of print]

Displacement of Submacular Hemorrhages in Age-Related Macular Degeneration with Subretinal Tissue Plasminogen Activator and Air.

Kadonosono K, Arakawa A, Yamane S, Inoue M, Yamakawa T, Uchio E, Yanagi Y.

OBJECTIVE: To study the anatomic and visual outcomes of a surgical procedure in which tissue plasminogen activator and air are injected subretinally to displace massive submacular hemorrhages secondary to age-related macular degeneration.

DESIGN: Prospective, consecutive, interventional case series.

PARTICIPANTS: Thirteen consecutive patients (13 eyes) with massive submacular hemorrhages secondary to age-related macular degeneration.

INTERVENTION: The surgical procedure consisted of a 25-gauge vitrectomy and submacular injection of tissue plasminogen activator (25 μg) and 0.4 ml air with a microneedle having an outer diameter of 50 μm. The procedure was followed by having the patient remain in the prone position overnight.

MAIN OUTCOME MEASURES: Mean visual acuity change from baseline, mean central lesion thickness change from baseline, fluorescein angiography findings, and surgical complications.

RESULTS: Total subfoveal blood displacement was achieved in all 13 eyes (100%). Central lesion thickness decreased from a mean baseline value of 867 μm to a mean value of 379 μm at 1 month after surgery. There was visual improvement in 11 eyes, no visual improvement in 1 eye, and poorer vision in 1 eye. The mean change in Early Treatment Diabetic Retinopathy Study letter score from baseline was 19.4 letters at 1 month (P = 0.006) and 23.3 letters at 3 months (P = 0.001). There was intraoperative macular hole formation.

CONCLUSIONS: Submacular air injection with a microneedle facilitates displacement of clots dissolved with tissue plasminogen activator with few complications and results in earlier visual improvement.

PMID: 25200400 [PubMed - as supplied by publisher]

Dev Ophthalmol. 2014;54:213-22. Epub 2014 Aug 26.

Subretinal hemorrhage.

Yiu G, Mahmoud TH.

Abstract: Large submacular hemorrhage (SMH) is a devastating complication of neovascular age-related

macular degeneration (AMD) that cannot be effectively managed with anti-vascular endothelial growth factor injections alone. While SMH is not common, AMD patients with existing coagulopathies or taking anticoagulant medications are particularly susceptible. Today, various techniques are available for the management of SMH, including pneumatic displacement with or without intravitreal tissue plasminogen activator (tPA), pars plana vitrectomy with subretinal tPA and gas tamponade, and submacular surgery with vitrectomy and retinotomy for clot extraction. While no consensus exists, the preferred technique is often determined by the extent or duration of the hemorrhage and surgeon preference. This chapter reviews treatment options for managing SMH, as well as the current evidence for supporting their use.

PMID: 25196772 [PubMed - in process]

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

CNGB3-achromatopsia clinical trial with CNTF: diminished rod pathway responses with no evidence of improvement in cone function.

Zein WM, Jeffrey BG, Wiley HE, Turriff AE, Tumminia SJ, Tao W, Bush RA, Marangoni D, Wen R, Wei LL, Sieving PA.

Purpose: Ciliary neurotrophic factor (CNTF) protects rod photoreceptors from retinal degenerative disease in multiple non-human models. Thus far, CNTF has failed to demonstrate rod protection in trials for human retinitis pigmentosa. Recently, CNTF was found to improve cone photoreceptor function in a canine CNGB3 achromatopsia model. This study explores whether this finding translates to humans with CNGB3 achromatopsia.

Methods: A 5 subject open-label Phase I/II study was initiated by implanting intraocular microcapsules releasing CNTF (nominally 20 ng/day) into one eye each of CNGB3 achromat participants. Fellow eyes served as untreated controls. Subjects were followed for one year.

Results: Pupil constriction in treated eyes gave evidence of intraocular CNTF release. Additionally, scotopic ERG responses were reduced, and dark adapted psychophysical absolute thresholds were increased, attributable to diminished rod or rod pathway activity. Optical coherence tomography revealed that the cone rich fovea underwent structural changes as the foveal hyporeflective zone (HRZ) became diminished in CNTF-treated eyes. No objectively measurable enhancement of cone function was found by assessments of visual acuity, mesopic increment sensitivity threshold or the photopic electroretinogram (ERG). Careful measurements of color hue discrimination showed no change. Nonetheless, subjects reported beneficial changes of visual function in the treated eyes, including reduced light sensitivity and aversion to bright light, which may trace to decreased effective ambient light from the pupillary constriction; further they noted slowed adaptation to darkness, consistent with CNTF action on rod photoreceptors.

Conclusions: CNTF did not measurably enhance cone function, which reveals a species difference between human and canine CNGB3 cones in responses to CNTF.

PMID: 25205868 [PubMed - as supplied by publisher]

Pathogenesis

Clin Ophthalmol. 2014 Aug 25;8:1573-8.

Evaluation of cardiovascular biomarkers in patients with age-related wet macular degeneration.

Keles S, Ates O, Kartal B, Alp HH, Ekinci M, Ceylan E, Ondas O, Arpali E, Dogan S, Yildirim K, Keles MS.

AIM: To evaluate levels of homocysteine, asymmetric dimethylarginine (ADMA), and nitric oxide (NO), as

well as activity of endothelial NO synthase (eNOS), in patients with age-related macular degeneration (AMD).

METHODS: The levels of homocysteine, ADMA, and NO and activity of eNOS in patients who were diagnosed with wet AMD by fundus fluorescein angiography (n=30) were compared to a control group with no retinal pathology (n=30).

RESULTS: Levels of homocysteine and ADMA were found to be significantly higher in the wet AMD group than in the control group (P<0.001), whereas NO levels and eNOS activity were higher in the control group (P<0.001). In the wet AMD group, we detected a 2.64- and 0.33-fold increase in the levels of ADMA and homocysteine, respectively, and a 0.49- and 2.41-fold decrease in the eNOS activity and NO level, respectively.

CONCLUSION: Elevated levels of homocysteine and ADMA were observed in patients with wet AMD. Increased ADMA may be responsible for the diminished eNOS activity found in these patients, which in turn contributes to the decrease in NO levels, which likely plays a role in the pathogenesis of AMD.

PMID: 25210424 [PubMed] PMCID: PMC4154890

Mediators Inflamm. 2014;2014:930671. Epub 2014 Aug 19.

Age-Related Macular Degeneration in the Aspect of Chronic Low-Grade Inflammation (Pathophysiological ParaInflammation).

Nita M, Grzybowski A, Ascaso FJ, Huerva V.

Abstract: The products of oxidative stress trigger chronic low-grade inflammation (pathophysiological parainflammation) process in AMD patients. In early AMD, soft drusen contain many mediators of chronic low-grade inflammation such as C-reactive protein, adducts of the carboxyethylpyrrole protein, immunoglobulins, and acute phase molecules, as well as the complement-related proteins C3a, C5a, C5, C5b-9, CFH, CD35, and CD46. The complement system, mainly alternative pathway, mediates chronic autologous pathophysiological parainflammation in dry and exudative AMD, especially in the Y402H gene polymorphism, which causes hypofunction/lack of the protective complement factor H (CFH) and facilitates chronic inflammation mediated by C-reactive protein (CRP). Microglial activation induces photoreceptor cells injury and leads to the development of dry AMD. Many autoantibodies (antibodies against alpha beta crystallin, alpha-actinin, amyloid, C1q, chondroitin, collagen I, collagen III, collagen IV, elastin, fibronectin, heparan sulfate, histone H2A, histone H2B, hyaluronic acid, laminin, proteoglycan, vimentin, vitronectin, and aldolase C and pyruvate kinase M2) and overexpression of Fcc receptors play role in immune-mediated inflammation in AMD patients and in animal model. Macrophages infiltration of retinal/choroidal interface acts as protective factor in early AMD (M2 phenotype macrophages); however it acts as proinflammatory and proangiogenic factor in advanced AMD (M1 and M2 phenotype macrophages).

PMID: 25214719 [PubMed - as supplied by publisher] PMCID: PMC4152952

Invest Ophthalmol Vis Sci. 2014 Sep 11.

γδ T cells as a major source of IL-17 production during age-dependent RPE degeneration.

Zhao Z, Xu P, Jie Z, Zuo Y, Yu B, Soong L, Sun J, Chen Y, Cai J.

Purpose: Chronic inflammation is a key factor contributing to the progression of age-related macular degeneration (AMD). The goals of the current study were to develop an improved mouse model with retinal pathological features similar to AMD and to characterize the immunoreactive cells in the outer retina and choroid during degeneration of the retinal pigment epithelium (RPE).

Methods: Mice deficient of nuclear erythroid 2-related factor 2 (Nrf2) at 12 months of age were fed with high fat, cholesterol-rich diet for up to 16 weeks. Ocular phenotype was monitored by optical coherence tomography (OCT) and scanning laser ophthalmoscopy (SLO) in live animals, and was further validated by retinal histopathology. Immunofluorescence staining of either cryosections or RPE flat mounts was used to define immunoreactive cells. Flow cytometry analyses were further performed to define the subsets of intraocular T lymphocytes.

Results: After 16 weeks on high fat (HF) diet, 58% of the eyes from Nrf2-/- mice had progression of retinal lesions. Major histocompatibility complex class II (MHC II)-positive microglias, Foxp3+ regulatory T cells (Tregs), and CD3+ IL-17-producing T cells were detected in either the retina or sub-RPE space. Flow cytometry analyses further revealed that most of the IL-17-producing cells were CD3+ CD4- TCRγδ+ cells.

Conclusions: The results suggest that the T cell-mediated immune responses played important roles in controlling the progression of AMD-like phenotype in Nrf2-deficient mice.

PMID: 25212781 [PubMed - as supplied by publisher]

J Med Chem. 2014 Sep 11. [Epub ahead of print]

Design, Synthesis, and Evaluation of Nonretinoid Retinol Binding Protein 4 Antagonists for the Potential Treatment of Atrophic Age-Related Macular Degeneration and Stargardt Disease.

Cioffi CL, Dobri N, Freeman EE, Conlon MP, Chen P, Stafford DG, Schwarz DM, Golden KC, Zhu L, Kitchen DB, Barnes KD, Racz B, Qin Q, Michelotti E, Cywin CL, Martin WH, Pearson PG, Johnson G, Petrukhin K.

Abstract: Accumulation of lipofuscin in the retina is associated with pathogenesis of atrophic age-related macular degeneration and Stargardt disease. Lipofuscin bisretinoids (exemplified by N-retinylidene-N-retinylethanolamine) seem to mediate lipofuscin toxicity. Synthesis of lipofuscin bisretinoids depends on the influx of retinol from serum to the retina. Compounds antagonizing the retinol-dependent interaction of retinol-binding protein 4 (RBP4) with transthyretin in the serum would reduce serum RBP4 and retinol and inhibit bisretinoid formation. We recently showed that A1120 (3), a potent carboxylic acid based RBP4 antagonist, can significantly reduce lipofuscin bisretinoid formation in the retinas of Abca4-/- mice. As part of the NIH Blueprint Neurotherapeutics Network project we undertook the in vitro exploration to identify novel conformationally flexible and constrained RBP4 antagonists with improved potency and metabolic stability. We also demonstrate that upon acute and chronic dosing in rats, 43, a potent cyclopentyl fused pyrrolidine antagonist, reduced circulating plasma RBP4 protein levels by approximately 60%.

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Hum Gene Ther Clin Dev. 2014 Sep 11. [Epub ahead of print]

Preclinical Safety Evaluation of a Recombinant AAV8 Vector for X-linked Retinoschisis after Intravitreal Administration in Rabbits.

Marangoni D1, Wu Z, Wiley HE, Zeiss CJ, Vijayasarathy C, Zeng Y, Hiriyanna S, Bush RA, Wei LL, Colosi P, Sieving PA.

Abstract: X-linked retinoschisis (XLRS) is a retinal disease caused by mutations in the gene encoding the protein retinoschisin (RS1) and one of the most common causes of macular degeneration in young men. Currently, no FDA approved treatments are available for XLRS and a replacement gene therapy could provide a promising strategy. We have developed a novel gene therapy approach for XLRS, based on the administration of AAV8-scRS/IRBPhRS, an adeno-associated viral vector coding the human RS1 protein, via the intravitreal route. On the basis of our prior study in a RS1-KO mouse, this construct transduces

efficiently all the retinal layers, resulting in a RS1 expression similar to that observed in the wild-type and improving retinal structure and function. In support of a clinical trial we carried out a study to evaluate the ocular safety of intravitreal administration of AAV8-scRS/IRBPhRS into 39 New Zealand rabbits. Two dose levels of vector, 2e10 and 2e11 vector genomes per eye (vg/eye) were tested and ocular inflammation was monitored over a 12-week period by serial ophthalmological and histopathological analysis. A mild ocular inflammatory reaction, consisting mainly of vitreous infiltrates, was observed within 4 weeks from injection, in both 2e10 and 2e11 vg/eye groups and was likely driven by the AAV8 capsid. At 12-week follow-up, ophthalmological examination revealed no clinical signs of vitreitis in both dose groups. However, while vitreous inflammatory infiltrate was significantly reduced in the 2e10 vg/eye group at 12 weeks, some rabbits in the higher dose group still showed persistence of inflammatory cells, histologically. In conclusion, intravitreal administration of AAV8-scRS/IRBPhRS into the rabbit eye produces a mild and transient intraocular inflammation that resolves, at a 2e10 vg/eye dose, within 3 months, and does not cause irreversible tissue damages. These data support the initiation of a clinical trial of intravitreal administration of AAV8-scRS/IRBPhRS in XLRS patients.

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Am J Pathol. 2014 Sep 6. [Epub ahead of print]

The Membrane Attack Complex in Aging Human Choriocapillaris: Relationship to Macular Degeneration and Choroidal Thinning.

Mullins RF, Schoo DP, Sohn EH, Flamme-Wiese MJ, Workamelahu G, Johnston RM, Wang K, Tucker BA, Stone EM.

Abstract: Age-related macular degeneration (AMD) is a common disease that can result in severe visual impairment. Abnormal regulation of the complement system has been implicated in its pathogenesis, and CFH polymorphisms contribute substantially to risk. How these polymorphisms exert their effects is poorly understood. We performed enzyme-linked immunosorbent assay (ELISA) analysis on young, aged, and AMD choroids to determine the abundance of the membrane attack complex (MAC) and performed immunofluorescence studies on eyes from 117 donors to evaluate the MAC in aging, early AMD, and advanced AMD. Morphometric studies were performed on eyes with high- or low-risk CFH genotypes. ELISA confirmed that MAC increases significantly with aging and with AMD. MAC was localized to Bruch's membrane and the choriocapillaris and was detectable at low levels as early as 5 years of age. Hard drusen were labeled with anti-MAC antibody, but large or confluent drusen and basal deposits were generally unlabeled. Labeling of retinal pigment epithelium was observed in some cases of advanced AMD, but not in early disease. Eyes homozygous for the high-risk CFH genotype had thinner choroids than low-risk homozygotes ($P < 0.05$). These findings suggest that increased complement activation in AMD and in high-risk genotypes can lead to loss of endothelial cells in early AMD. Treatments to protect the choriocapillaris in early AMD are needed.

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Mol Neurobiol. 2014 Sep 10. [Epub ahead of print]

Beta-Amyloid Precursor Protein (βAPP) Processing in Alzheimer's Disease (AD) and Age-Related Macular Degeneration (AMD).

Zhao Y, Bhattacharjee S, Jones BM, Hill JM, Clement C, Sambamurti K, Dua P, Lukiw WJ.

Abstract: Amyloid is a generic term for insoluble, often intensely hydrophobic, fibrous protein aggregates that arise from inappropriately folded versions of naturally-occurring polypeptides. The abnormal generation and accumulation of amyloid, often referred to as amyloidogenesis, has been associated with the immune

and pro-inflammatory pathology of several progressive age-related diseases of the human central nervous system (CNS) including Alzheimer's disease (AD) and age-related macular degeneration (AMD). This 'research perspective' paper reviews some of the research history, biophysics, molecular-genetics and environmental factors concerning the contribution of amyloid beta (Aβ) peptides, derived from beta-amyloid precursor protein (βAPP), to AD and AMD that suggests an extensive similarity in immune and inflammatory degenerative mechanisms between these two CNS diseases.

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PLoS One. 2014 Sep 9;9(9):e107461.

A Circulating MicroRNA Profile Is Associated with Late-Stage Neovascular Age-Related Macular Degeneration.

Grassmann F, Schoenberger PG, Brandl C, Schick T, Hasler D, Meister G, Fleckenstein M, Lindner M, Helbig H, Fauser S, Weber BH.

Abstract: Age-related macular degeneration (AMD) is the leading cause of severe vision impairment in Western populations over 55 years. A growing number of gene variants have been identified which are strongly associated with an altered risk to develop AMD. Nevertheless, gene-based biomarkers which could be dysregulated at defined stages of AMD may point toward key processes in disease mechanism and thus may support efforts to design novel treatment regimens for this blinding disorder. Circulating microRNAs (cmiRNAs) which are carried by nanosized exosomes or microvesicles in blood plasma or serum, have been recognized as valuable indicators for various age-related diseases. We therefore aimed to elucidate the role of cmiRNAs in AMD by genome-wide miRNA expression profiling and replication analyses in 147 controls and 129 neovascular AMD patients. We identified three microRNAs differentially secreted in neovascular (NV) AMD (hsa-mir-301-3p, pcorrected=5.6*10-5, hsa-mir-361-5p, pcorrected=8.0*10-4 and hsa-mir-424-5p, pcorrected=9.6*10-3). A combined profile of the three miRNAs revealed an area under the curve (AUC) value of 0.727 and was highly associated with NV AMD (p=1.2*10-8). To evaluate subtype-specificity, an additional 59 AMD cases with pure unilateral or bilateral geographic atrophy (GA) were analyzed for microRNAs hsa-mir-301-3p, hsa-mir-361-5p, and hsa-mir-424-5p. While we found no significant differences between GA AMD and controls neither individually nor for a combined microRNAs profile, hsa-mir-424-5p levels remained significantly higher in GA AMD when compared to NV (pcorrected<0.005). Pathway enrichment analysis on genes predicted to be regulated by microRNAs hsa-mir-301-3p, hsa-mir-361-5p, and hsa-mir-424-5p, suggests canonical TGFβ, mTOR and related pathways to be involved in NV AMD. In addition, knockdown of hsa-mir-361-5p resulted in increased neovascularization in an in vitro angiogenesis assay.

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PLoS One. 2014 Sep 8;9(9):e106610. eCollection 2014.

A novel form of progressive retinal atrophy in Swedish vallhund dogs.

Cooper AE, Ahonen S, Rowlan JS, Duncan A, Seppälä EH, Vanhapelto P, Lohi H, Komáromy AM.

Abstract: Inherited retinal degenerations, such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD), represent leading causes of incurable blindness in humans. This is also true in dogs, where the term progressive retinal atrophy (PRA) is used to describe inherited photoreceptor degeneration resulting in progressive vision loss. Because of the similarities in ocular anatomy, including the presence of a cone photoreceptor-rich central retinal region, and the close genotype-phenotype correlation, canine models contribute significantly to the understanding of retinal disease mechanisms and the development of new therapies. The screening of the pure-bred dog population for new forms of PRA represents an

important strategy to establish new large animal models. By examining 324 dogs of the Swedish vallhund breed in seven countries and across three continents, we were able to describe a new and unique form of PRA characterized by the multifocal appearance of red and brown discoloration of the tapetal fundus followed over time by thinning of the retina. We propose three stages of the disease based on the appearance of the ocular fundus and associated visual deficits. Electroretinography revealed a gradual loss of both rod and cone photoreceptor-mediated function in Stages 2 and 3 of the disease. In the few dogs that suffered from pronounced vision loss, night-blindness occurred first in late Stage 2, followed by decreased day-vision in Stage 3. Histologic examinations confirmed the loss of photoreceptor cells at Stage 3, which was associated with the accumulation of autofluorescent material in the adjacent retinal pigment epithelium. Pedigree analysis was suggestive of an autosomal-recessive mode of inheritance. Mutations in six known canine retinal degeneration genes as well as hypovitaminosis E were excluded as causes of the disease. The observed variability in the age of disease onset and rate of progression suggest the presence of genetic and/or environmental disease modifiers.

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Epidemiology

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

METABOLIC SYNDROME AND RISK OF AGE-RELATED MACULAR DEGENERATION.

Ghaem Maralani H, Tai BC, Wong TY, Tai ES, Li J, Wang JJ, Mitchell P.

PURPOSE: To investigate the relationship between metabolic syndrome (MetS) and its components with the risk of early- and late-stage age-related macular degeneration (AMD).

METHODS: A prospective cohort of individuals aged older than or equal to 49 years were followed up over a period of 10 years in the Blue Mountains Eye Study, Australia. MetS components were measured at baseline (1992-1994), 5-year (1997-1999), and 10-year (2002-2004) follow-ups. Incident cases of early and late AMD were diagnosed using standard photographic grading of retinal images of 2,218 participants at risk. Mixed-effect logistic regression was conducted to explore the relationship between MetS (and its components) with subsequent development of early/late AMD.

RESULTS: Over the 10-year follow-up, early AMD developed in 12% and late AMD in 3% of participants at risk. Amongst subjects aged younger than or equal to 70 years, MetS was associated with the incidence of late AMD. Of the five MetS components, obesity, high glucose, and high triglyceride were associated with the increased incidence of late AMD during the 10-year follow-up. There was no evidence of effect of MetS and its components on the risk of early AMD.

CONCLUSION: Metabolic syndrome, obesity, high glucose, and high triglycerides were predictors of progression to late AMD. These data provide additional insights into the pathogenesis of AMD.

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Genetics

Cold Spring Harb Perspect Med. 2014 Sep 11. [Epub ahead of print]

Genome-Wide Association Studies: Getting to Pathogenesis, the Role of Inflammation/Complement in AMD.

Cooke Bailey JN, Pericak-Vance MA, Haines JL.

Abstract: Age-related macular degeneration (AMD) is a chronic, degenerative, and significant cause of visual impairment and blindness in the elderly. Genetic and epidemiological studies have confirmed that AMD has a strong genetic component, which has encouraged the application of increasingly sophisticated genetic techniques to uncover the important underlying genetic variants. Although various genes and pathways have been implicated in the risk for AMD, complement activation has been emphasized repeatedly throughout the literature as having a major role both physiologically and genetically in susceptibility to and pathogenesis of this disease. This article explores the research efforts that brought about the discovery and characterization of the role of inflammatory and immune processes (specifically complement) in AMD. The focus herein is on the genetic evidence for the role of complement in AMD as supported specifically by genome-wide association (GWA) studies, which interrogate hundreds of thousands of variants across the genome in a hypothesis-free approach, and other genetic interrogation methods.

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

Genetic determinants of age-related macular degeneration in diverse populations from the PAGE Study.

Restrepo NA, Spencer KM, Goodloe R, Garrett TA, Heiss G, Bůžková P, Jorgensen N, Jensen RA, Matise TC, Hindorff LA, Klein BE, Klein R, Wong TY, Cheng CY, Cornes BK, Tai ES, Ritchie MD, Haines J, Crawford DC.

Purpose: Substantial progress has been made in identifying susceptibility variants for age-related macular degeneration (AMD) in European populations; however, few studies have been conducted to understand the role these variants play in AMD risk in diverse populations. The present study aims to examine AMD risk across diverse populations in known and suspected AMD complement factor and lipid-related loci.

Methods: Targeted genotyping was performed across study sites for AMD and lipid trait-associated SNPs. Genetic association tests were performed at individual sites and then meta-analyzed using logistic regression assuming an additive genetic model stratified by self-described race/ethnicity to determine risk of any AMD. Participants included cases with early or late AMD and controls with no signs of AMD as determined by fundus photography. Populations included in this study were European Americans, African Americans, Mexican Americans, and Singaporeans from the Population Architecture using Genomics and Epidemiology (PAGE) study.

Results: AMD index variants rs1061170 (CFH) and rs10490924 (ARMS2) were associated with AMD at p=3.05x10-8 and p=6.36x10-6, respectively, in European Americans. In general, none of the major AMD index variants generalized to our non-European populations with the exception of rs10490924 in Mexican Americans (p<0.05). Four lipid-associated SNPs (LPL rs328, TRIB1 rs6987702, CETP rs1800775, and KCTD10/MVK rs2338104) were associated with AMD in African Americans and Mexican Americans at a liberal significance threshold (p<0.05).

Conclusions: While most associations did not generalize in the non-European populations, variants within lipid-related genes were found to be associated with AMD. This study highlights the need for larger well-powered studies in non-European populations.

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Diet & lifestyle

J Trace Elem Med Biol. 2014 Aug 12. [Epub ahead of print]

Zinc: An antioxidant and anti-inflammatory agent: Role of zinc in degenerative disorders of aging.

Prasad AS.

Abstract: In the developed countries nearly 30% of the elderly are zinc deficient. Many chronic diseases seen in the elderly such as atherosclerosis, diabetes, neuro-degenerative disorders, Parkinson's disease and age related macular degeneration (AMD) may be due to chronic inflammation and increased oxidative stress. Zinc in human plays an important role in cell mediated immunity and is also an antioxidant and anti-inflammatory agent. Zinc supplementation studies in the elderly have shown decreased incidence of infections, decreased oxidative stress, and decreased generation of inflammatory cytokines. Decreased incidences of blindness in patients with AMD and increased atheroprotective effect have been observed in the zinc supplemented elderly. Zinc is a molecular signal for immune cells and many transcription factors involved in gene expression of inflammatory cytokines and adhesion molecules are regulated by zinc.

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Ophthalmology. 2014 Sep 4. [Epub ahead of print]

Treatment Response to Antioxidants and Zinc Based on CFH and ARMS2 Genetic Risk Allele Number in the Age-Related Eye Disease Study.

Awh CC, Hawken S, Zanke BW.

OBJECTIVE: To evaluate the impact of complement factor H (CFH) and age-related maculopathy susceptibility 2 (ARMS2) risk alleles on the observed response to components of the Age-Related Eye Disease Study (AREDS) formulation.

DESIGN: Genetic and statistical subgroup analysis of a randomized, prospective clinical trial.

PARTICIPANTS: White patients from the AREDS with category 3 or 4 age-related macular degeneration (AMD) with available DNA (n = 989).

METHODS: Four genotype groups based on CFH and ARMS2 risk allele number were defined. Progression to advanced AMD was analyzed by genotype and treatment using Cox proportionate hazards estimates and 7-year events.

MAIN OUTCOME MEASURES: The effect of predefined genotype group on treatment-specific progression to advanced AMD.

RESULTS: Patients with 2 CFH risk alleles and no ARMS2 risk alleles progressed more with zinc-containing treatment compared with placebo, with a hazard ratio (HR) of 3.07 (P = 0.0196) for zinc and 2.73 (P = 0.0418) for AREDS formulation (AF). Seven-year treatment-specific progression rates were: placebo, 17.0%; zinc, 43.2% (P = 0.023); and AF, 40.2% (P = 0.039). Patients with 0 or 1 CFH risk alleles and 1 or 2 ARMS2 risk alleles benefited from zinc-containing treatment compared with placebo, with an HR of 0.514 for zinc (P = 0.012) and 0.569 for AF (P = 0.0254). Seven-year treatment-specific AMD progression rates were as follows: placebo, 43.3%; zinc, 25.2% (P = 0.020); and AF, 27.3% (P = 0.011). Zinc and AF treatment each interacted statistically with these 2 genotype groups under a Cox model, with P values of 0.000999 and 0.00366, respectively. For patients with 0 or 1 CFH risk alleles and no ARMS2 risk alleles, neither zinc-containing treatment altered progression compared with placebo, but treatment with antioxidants decreased progression (HR, 0.380; P = 0.034). Seven-year progression with placebo was 22.6% and with antioxidants was 9.17% (P = 0.033). For patients with 2 CFH risk alleles and 1 or 2 ARMS2 risk alleles, no treatment was better than placebo (48.4%).

CONCLUSIONS: The benefit of the AREDS formulation seems the result of a favorable response by patients in only 1 genotype group, balanced by neutral or unfavorable responses in 3 genotype groups.

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Cutan Ocul Toxicol. 2014 Sep 8:1-5. [Epub ahead of print]

Effects of cigarette smoking on choroidal and retinal thickness and ocular pulse amplitude.

Dervişoğulları MS, Totan Y, Tenlik A, Yuce A.

Background: In our study, we aimed to show the effects of smoking on choroidal thickness and ocular pulse amplitude. It is known that the anatomy and physiologic functions of the choroid is important in ocular diseases like glaucoma and age-related macular degeneration. Choroidal thickness is measured by the spectral domain optical coherence tomography (SD-OCT). The ocular pulse amplitude (OPA) is the difference between the systolic and diastolic intraocular pressure (IOP) and it is an index of choroidal perfusion.

Design: This was a cross-sectional prospective observational study at the Turgut Ozal University Hospital setting.

Participants: The test subjects were divided into two groups: the smokers group which consisted in 24 participants (20 male, 4 female) and the control group with 22 participants (16 male, 6 female).

Methods: The participants underwent full ophthalmological examination including best-corrected visual acuity (BCVA), spherical equivalent (SE) values of refractive errors, intraocular pressure (IOP), ocular pulse amplitude (OPA), central corneal thickness (CCT), axial length (AL) and choroidal thickness. The IOP and the OPA were measured with the dynamic contour tonometer. The CCT and the AL were measured with the Nidek AL-Scan (Nidek Co., Ltd., Gamagori, Japan). The choroidal thickness was measured by the Cirrus high-definition optical coherence tomography (Cirrus Version 6.0; Carl Zeiss Meditec, Dublin, CA).

Results: Gender did not differ significantly between the groups ($p = 0.12$). The age, SE, IOP, OPA, CCT and AL did not differ significantly in smokers and control groups ($p = 0.12$, $p = 0.37$, $p = 0.54$, $p = 0.80$, $p = 0.56$ and $p = 0.82$, respectively). The nasal, temporal, central retinal ($p = 021$, $p = 021$, $p = 0.11$) and nasal, temporal, central choroidal thicknesses ($p = 0.80$, $p = 0.39$, $p = 0.75$) did not differ significantly between smokers and control groups.

Conclusions: We could not find a significant difference in OPA, retinal and choroidal thicknesses between smokers and non smokers. Further studies including histopathological changes in larger groups are needed to show the effect of smoking on choroidal thickness especially in patients with ocular diseases like age-related macular degeneration.

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Eur J Ophthalmol. 2014 Sep 4:0. [Epub ahead of print]

Effect of the blue filter intraocular lens on the progression of geographic atrophy.

Pipis A, Touliou E, Pillunat LE, Augustin AJ.

PURPOSE: To clinically evaluate the effect of blue light-filtering intraocular lenses (IOLs) on disease progression in patients with geographic atrophy (GA).

METHODS: Clinical data from 66 eyes of 40 patients were investigated, 27 with a blue filter and 39 with a non-blue filter IOL. Spectral-domain optical coherence tomography technology and the advanced retinal pigment epithelium analysis software tool were used to measure lesion size and monitor its progression over 1 year.

RESULTS: The mean and median baseline area of GA for the total sample was 5.55 ± 4.72 mm2 and 4.40 mm2, respectively. There was a statistically significant difference of the mean ($p = 0.0002$) and median ($p<0.0001$) GA progression in 1 year between the blue filter and non-blue filter IOL group (0.72 ± 0.39 SD mm2 mean and 0.70 mm2 median compared to 1.48 ± 0.88 SD mm2 and 1.30 mm2, respectively).

CONCLUSIONS: The clinical data strongly support a photoprotective role of blue light-filtering IOLs on the progression of the atrophic form of dry age-related macular degeneration after cataract surgery.

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Optom Vis Sci. 2014 Sep 11. [Epub ahead of print]

Do Blue-Light Filtering Intraocular Lenses Affect Visual Function?

Lavric A, Pompe MT.

PURPOSE: To study different aspects of visual function, macular changes, and subjective differences between the eye with an ultraviolet (UV) and blue-light filtering intraocular lens (IOL) and the fellow eye with a UV-light filtering IOL.

METHODS: Thirty patients (60 eyes) with senile cataract had both cataracts extracted, and an IOL was implanted at least 2 years before clinical evaluation. In one eye, AcrySof SA60AT (a UV-light filtering IOL) was implanted, whereas in the contralateral eye, AcrySof IQ SN60WF (a blue-light filtering IOL) was implanted. Each patient underwent visual acuity testing, color vision testing (Ishihara and Farnsworth-Munsell 100-hue tests), and contrast sensitivity (CS) testing. The macula was evaluated with optical coherence tomography and with clinical examination. Patients were asked if they noted any difference between the implanted IOLs concerning visual impression. Subjective visual quality was evaluated using the National Eye Institute Visual Functioning Questionnaire.

RESULTS: There was a borderline statistically significant difference in the mean best-corrected visual acuity ($p = 0.05$). As regards color vision, no significant changes in Ishihara and Farnsworth-Munsell 100-hue error scores were detected between both eyes ($p = 0.48$ and $p = 0.59$, respectively). Analysis of CS showed no significant difference between the groups at any spatial frequency. There were also no statistically significant differences in central macular thickness and total macular volume between the two IOL groups ($p = 0.72$ and $p = 0.61$, respectively). In both IOL groups, three eyes developed an epiretinal membrane, and six eyes developed early signs of age-related macular degeneration.

CONCLUSIONS: This study showed no significant effects of a blue-light filtering IOL on visual acuity and no influence on color perception and CS. After more than 2 years, there were no significant differences in macular changes between the IOL groups. Clinical evidence of the effect of a blue-light filtering IOL on macular protection is still lacking.

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