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MD Research News

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Drug Treatment

Am J Ophthalmol. 2010 Dec 17. [Epub ahead of print]

Survey of Intravitreal Injection Techniques Among Retinal Specialists in the United States.

Green-Simms AE, Ekdawi NS, Bakri SJ.

Abstract

PURPOSE: To describe the intravitreal injection technique practice patterns of retinal specialists in the United States from April 8, 2010 to April 21, 2010.

DESIGN: Questionnaire survey.

METHODS: All members of the American Academy of Ophthalmology who self-categorized as "Retinal/Vitreous Surgery" were contacted by e-mail to complete an anonymous, 20-question, internet-based survey.

RESULTS: A total of 765 retinal specialists (44%) responded to the survey. Most respondents wear gloves (58%) and use an eyelid speculum (92%) when performing an intravitreal injection. More than 99% use povidone-iodine preinjection. The majority measure the injection site from the limbus (56%) and inject straight into the vitreous cavity (96%). Most do not displace the conjunctiva (83%). Seventy-two percent routinely assess postinjection optic nerve perfusion, primarily by gross visual acuity measurement (32%). While nearly one third of participants use prophylactic topical antibiotics preinjection, more than two thirds use topical antibiotics postinjection. Forty-six percent perform bilateral simultaneous intravitreal injections. The majority of respondents use a 30-gauge needle for the injection of ranibizumab (78%) and bevacizumab (60%). However, respondents use both a 27- and 30-gauge needle for the injection of triamcinolone acetonide.

CONCLUSIONS: Retinal specialists in the United States participate in a range of techniques for the care before, during, and after intravitreal injections. Further study is needed to elucidate best practice patterns.

PMID: 21168821 [PubMed - as supplied by publisher]

Eye (Lond). 2010 Dec 24. [Epub ahead of print]

The role of anti-inflammatory agents in age-related macular degeneration (AMD) treatment.

Wang Y, Wang VM, Chan CC.

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Health, Bethesda, MD, USA [2] Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China.

Abstract

Although age-related macular degeneration (AMD) is not a classic inflammatory disease like uveitis, inflammation has been found to have an important role in disease pathogenesis and progression. Innate immunity and autoimmune components, such as complement factors, chemokines, cytokines, macrophages, and ocular microglia, are believed to be heavily involved in AMD development. Targeting these specific inflammatory molecules has recently been explored in an attempt to better understand and treat AMD. Although antivascular endothelial growth factor therapy is the first line of defence against neovascular AMD, anti-inflammatory agents such as corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), immunosuppressive agents (eg, methotrexate and rapamycin), and biologics (eg, infliximab, daclizumab, and complement inhibitors) may provide an adjunct or alternative mechanism to suppress the inflammatory processes driving AMD progression. Further investigation is required to evaluate the long-term safety and efficacy of these drugs for both neovascular and non-neovascular AMD.Eye advance online publication, 24 December 2010; doi:10.1038/eye.2010.196.

PMID: 21183941 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2010 Dec 22. [Epub ahead of print]

Preferential hyperacuity perimeter in assessing responsiveness to ranibizumab therapy for exudative age-related macular degeneration.

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Abstract

Aim: To investigate the ability of the preferential hyperacuity perimeter test to assess responsiveness to ranibizumab therapy for exudative age-related macular degeneration (AMD).

Methods Fourteen consecutive patients with newly diagnosed choroidal neovascularisation underwent a preferential hyperacuity perimeter metamorphopsia test (main outcome measures) 1 h before (baseline) and 1 h, 1 day, 1 week and 1 month after one intravitreal injection of ranibizumab (0.05 ml/0.5 mg). Best corrected visual acuity (BCVA) and several spectral domain optical coherence tomography (OCT) parameters (secondary outcome measures) were compared with the metamorphopsia test.

Results Fourteen eyes (14 patients, 78% women, mean age 83±6.2 years) were included in the analysis. The mean preferential hyperacuity perimeter metamorphopsia test score improved significantly from 20.4±35 at baseline to 9.2±23 after the single ranibizumab injection ($p<0.05$). The mean reduction in central macular thickness, maximal retinal thickness at the fovea, maximal height of subretinal fluid, maximal diameter of the largest retinal cyst and maximal height of pigment epithelial detachment, as evaluated by spectral domain OCT, closely reflected the functional improvements as evaluated by preferential hyperacuity perimeter, showing a significant correlation with metamorphopsia changes (Spearman correlation 0.9, $p<0.05$). Mean BCVA improved significantly from 20/80 to 20/60 ($p<0.05$). A significant correlation was also found between the mean BCVA changes and the mean metamorphopsia changes (Spearman correlation 0.97, $p<0.05$). The correlation coefficient between OCT measurements and preferential hyperacuity perimeter score within subjects was 0.51 ($p<0.05$).

Conclusion The improvement in metamorphopsia test score after intravitreal ranibizumab injection, which correlated closely with improvement in several OCT parameters, suggests that the preferential hyperacuity perimeter test may be used to monitor the response to anti-vascular endothelial growth factor (VEGF) treatment in patients with exudative AMD.

PMID: 21183512 [PubMed - as supplied by publisher]

Retina. 2010 Dec 21. [Epub ahead of print]

INCIDENCE OF ENDOPHTHALMITIS AFTER INTRAVITREAL INJECTION OF ANTIVASCULAR ENDOTHELIAL GROWTH FACTOR MEDICATIONS USING TOPICAL LIDOCAINE GEL ANESTHESIA.

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From the *Southeastern Retina Associates, Knoxville, Tennessee; and †Department of Surgery, Graduate School of Medicine, University of Tennessee, Knoxville, Tennessee.

PURPOSE: The purpose of this study was to determine the incidence of infectious endophthalmitis after intravitreal injection of antivascular endothelial growth factor medications using 2% topical lidocaine gel anesthesia.

METHODS: Retrospective chart review of 4690 consecutive intravitreal injections of antivascular endothelial growth factor medications using 2% topical lidocaine gel anesthesia. All patients had at least 6 weeks of follow-up.

RESULTS: A total of 608 patients underwent intravitreal injection of antivascular endothelial growth factor medications during the study period. There were 428 injections of pegaptanib sodium, 1841 injections of bevacizumab, and 2421 injections of ranibizumab. There were no cases of infectious endophthalmitis. The per-injection infection rate was 0.0% (95% confidence interval, 0.0-0.06%).

CONCLUSION: The incidence of infectious endophthalmitis after intravitreal injection of antivascular endothelial growth factor medications using 2% topical lidocaine gel anesthesia is low.

PMID: 21178659 [PubMed - as supplied by publisher]

Eur J Pharm Biopharm. 2010 Dec 17. [Epub ahead of print]

Association of ranibizumab (Lucentis®) or bevacizumab (Avastin®) with dexamethasone and triamcinolone acetonide: an in-vitro stability assessment.

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Abstract

The in-vitro stability of monoclonal antibodies used for age-related macular degeneration, ranibizumab and bevacizumab, was investigated. The aggregation profile of the antibodies was compared, alone and after association with dexamethasone sodium phosphate or triamcinolone acetonide. Commercial formulations of ranibizumab and bevacizumab were dialysed into three different buffers. After dialysis, samples were stored at 4°C, 25°C and 40°C during 35 days, alone and in combination with dexamethasone sodium phosphate, triamcinolone acetonide phosphate solution or triamcinolone acetonide suspension. Combined formulations based on both commercial formulations were investigated as well. The aggregation state of the antibodies was measured by multi-angle light scattering (MALS) after separation by asymmetrical flow field-flow fractionation (AFFF) or size-exclusion chromatography (SEC). Ranibizumab results to be more stable than bevacizumab, alone and in combination with dexamethasone sodium phosphate or triamcinolone acetonide. Elevation in concentration, pH and temperature causes a decrease in stability of both antibodies. The association of triamcinolone acetonide phosphate solution with either ranibizumab or bevacizumab is observed to be the least stable combination of all samples tested. Dexamethasone sodium phosphate was shown to have a stabilizing effect on bevacizumab, although this is not the case for its combination with the commercial formulation Avastin®. The results demonstrate that the in-vitro association of either ranibizumab or bevacizumab with dexamethasone sodium phosphate or triamcinolone acetonide suspension does not decrease the stability of these antibodies. Although ranibizumab is more stable than bevacizumab in-vitro, further research has to point out how this affects their mechanism of action in vivo.

PMID: 21172437 [PubMed - as supplied by publisher]

Arch Biochem Biophys. 2010 Dec 17. [Epub ahead of print]

Ophthalmologe. 2010 Dec 19. [Epub ahead of print]

[Early treatment of exudative age-related macular degeneration with ranibizumab (Lucentis®) : The key to success.] [Article in German]

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BACKGROUND: Intravitreal ranibizumab (Lucentis®) is an effective treatment for exudative age-related macular degeneration (AMD). Up to now, settlement for this therapy remains quite complex and is handled differently by insurance companies as well as in the different German states. Often applications must be submitted and approved before an injection can be made. This procedure is time consuming and a delay in starting treatment might result. The aim of this study was to determine the effect of late-onset injection on visual acuity before and during the upload procedure.

METHODS: All patients treated with ranibizumab intravitreally between February 2007 and May 2010 were retrospectively evaluated for their best-corrected visual acuity at the day of diagnosis, injections during the upload phase and first follow-up visit after upload.

RESULTS: A total of 1,149 eyes were evaluated and divided into 2 groups according to time between diagnosis and first injection (group 1: =10 days, group 2: >10 days). There was no statistically significant difference between the groups for average age, gender, visual acuity at day of diagnosis and type of choroidal neovascularisation. However, both groups differed in the loss of visual acuity before the first injection and the possible increase in visual acuity. Group 1 waiting =10 days showed - in contrast to group 2 waiting >10 days - a smaller loss of visual acuity before upload and greater gain of visual acuity during upload. Those differences were statistically significant.

CONCLUSION: Successful treatment of exudative AMD requires small intervals between diagnosis and first ranibizumab injection. After diagnosis, the first injection with ranibizumab should be given as early as possible.

PMID: 21170652 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2010 Dec 18. [Epub ahead of print]

Individual recurrence intervals after anti-VEGF therapy for age-related macular degeneration.

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BACKGROUND: To assess the time interval to recurrent choroidal neovascular membrane (CNV) activity in eyes with neovascular age-related macular degeneration (AMD) after intravitreal anti-VEGF therapy.

METHODS: Data from all patients who received intravitreal ranibizumab injections for neovascular AMD at the University of Cologne prior to February 2009 were retrospectively reviewed. Patients were treated on a pro re nata (PRN) basis and eyes with active CNV received three consecutive monthly injections. Recurrence of CNV activity was defined as recurrence of intra- or subretinal fluid on optical coherence tomography (OCT) or leakage on fluorescein angiography (FA) after initial resolution of fluid and leakage following anti-VEGF therapy. All eyes showing at least two documented recurrences of CNV activity during follow-up were included in this analysis. Recurrence intervals were calculated and were deemed to be regular or periodical if the difference between recurrence interval times was less than 50 days.

RESULTS: Twenty-nine eyes of 28 patients met the inclusion criteria. Two to six recurrences were detected per case (mean 2.8 ± 1.1 recurrences). Recurrence intervals ranged from 41 days to 523 days (mean 5.5? ±?3.4 months, median 4.5 months). Twenty-two eyes (76%) showed at least two periodical recurrence intervals. In 12 eyes (41%), all recurrences occurred at regular intervals (2-4 recurrences, mean 2.3 ± 0.6 recurrences). Seven eyes (24%) showed irregular recurrence intervals (2-3 recurrences, mean 2.1 ± 0.4 recurrences). All 11 eyes with a classic CNV lesion component showed at least two periodical recurrence intervals. Eyes with occult CNV lesions showed periodical recurrence intervals in 11 out of 18 cases (61%).

CONCLUSIONS: Preliminary data indicate that periodical recurrences of CNV activity may be seen in eyes with neovascular AMD undergoing anti-VEGF therapy. Knowledge of individual recurrence interval times may allow for the development of an individualized treatment plan and prophylactic therapy.

PMID: 21170547 [PubMed - as supplied by publisher]

Arch Soc Esp Oftalmol. 2010 Oct;85(10):329-332. Epub 2010 Nov 3.

[Morphometric analysis of corneal endothelium after intravitreal ranibizumab (Lucentis(®)) in age-related macular degeneration treatment.] [Article in Spanish]

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PURPOSE: To determine the effect of intravitreal injection of 0.5mg ranibizumab on the corneal endothelium in patients with age-related macular degeneration (AMD).

METHODS: Observational, prospective case series pilot study. Twenty-six eyes of 26 consecutive patients with AMD were evaluated. All participants received one monthly intravitreal injections of 0.5mg ranibizumab for three consecutive months. The follow-up period was 6 months. Central corneal specular microscopy was performed before injection and at 7 days and 6 months after the first intravitreal injection. The endothelial cell density, coefficient of variation of cell size, and percentage of hexagonal cells were analyzed and the central corneal thickness was measured.

RESULTS: There were no significant differences in the endothelial cell densities, coefficients of variation of cell size and percentages of hexagonal cells before injection and at 7 days and 6 months after the first intravitreal ranibizumab injection (P>0.5). There was also no significant difference in central corneal thickness measurements through the follow-up period (P>0.5).

CONCLUSIONS: Repeated intravitreal injections of 0.5mg ranibizumab do not seem to cause substantial changes in the corneal endothelium.

PMID: 21168057 [PubMed - as supplied by publisher]Free Article

Drug Discov Today. 2010 Dec 14. [Epub ahead of print]

Drug delivery to the posterior segment of the eye.

Thrimawithana TR, Young S, Bunt CR, Green C, Alany RG.

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Abstract

Delivery of drugs to the posterior eye is challenging, owing to anatomical and physiological constrains of the eye. There is an increasing need for managing rapidly progressing posterior eye diseases, such as age-related macular degeneration, diabetic retinopathy and retinitis pigmentosa. Drug delivery to the posterior segment of the eye is therefore compounded by the increasing number of new therapeutic entities (e.g.

oligonucleotides, aptamers and antibodies) and the need for chronic therapy. Currently, the intravitreal route is widely used to delivery therapeutic entities to the retina. However, frequent administration of drugs via this route can lead to retinal detachment, endophthalmitis and increased intraocular pressure. Various controlled delivery systems, such as biodegradable and non-biodegradable implants, liposomes and nanoparticles, have been developed to overcome such adverse effects, with some success. The periocular route is a promising alternative, owing to the large surface area and the relatively high permeability of the sclera. Yet, the blood-retinal barrier and efflux transporters hamper the transport of therapeutic entities to the retina. As such, the efficient delivery of drugs to the posterior eye remains a major challenge facing the pharmaceutical scientist. In this review, we discuss the barriers to posterior eye drug delivery and the various drug-delivery strategies used to overcome these barriers.

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Am J Ophthalmol. 2010 Dec 17. [Epub ahead of print]

Intravitreal Injection Anesthesia-Comparison of Different Topical Agents: A Prospective Randomized Controlled Trial.

Yau GL, Jackman CS, Hooper PL, Sheidow TG.

PURPOSE: To compare the anesthetic effectiveness of 3 topical agents used for intravitreal injections.

DESIGN: Randomized, triple-armed, double-blinded, prospective, single-centered trial in patients receiving intravitreal ranibizumab for neovascular age-related macular degeneration.

METHODS: Patients were randomized 1:1:1 to receive 0.5% tetracaine hydrochloride drops and a 4% lidocaine pledget (n = 31), 0.5% tetracaine hydrochloride drops alone (n = 31), or 4% cocaine (+ epinephrine 1/100 000) drops alone (n = 31). Patients were asked to score their pain experience using a visual analogue scale (VAS) immediately following and 15 minutes after their injection. The average of these scores was used as the primary outcome. The physician performing the procedure separately scored his perception of the patients' pain using the Wong-Baker FACES scale.

RESULTS: Means of the averaged VAS pain score for Groups 1, 2, and 3 were: 19 (95% confidence interval [CI] 12-26), 21 (95% CI 13-29), and 21 (95% CI 16-27) respectively. Mean Wong-Baker pain scores for Groups 1, 2, and 3 were 1.9 (95% CI 1.3-2.6), 2.1 (95% CI 1.4-2.7), and 2.3 (95% CI 1.6-3.1) respectively. There was no significant difference (P = .549) between groups for average VAS pain score. Similarly, there was no significant difference (P = .790) for the physician-perceived pain score between groups.

CONCLUSIONS: There was no clinical difference in patient pain experience between the 3 anesthetic options tested. The addition of a 4% lidocaine pledget offered no clinical advantage in pain relief compared to 0.5% tetracaine or 4% cocaine (+ epinephrine 1/100 000) drops alone.

PMID: 21168822 [PubMed - as supplied by publisher]

J Mol Med. 2010 Dec 18. [Epub ahead of print]

Emerging therapeutic approaches in the management of retinal angiogenesis and edema.

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Abstract

Conditions resulting in retinal angiogenesis and edema (exudative age-related macular degeneration, diabetic retinopathy, retinal vein occlusion and retinopathy of prematurity) are major causes of visual

impairment, with significant impact on quality of life. There has been increasing clinical usage of anti-vascular endothelial growth factor (anti-VEGF) agents to stop retinal angiogenesis and resolve intraretinal fluid arising from these conditions. However, anti-VEGFs have not been completely successful in curing these conditions, and a range of emerging treatments aimed at supplementing or competing with anti-VEGF agents are being developed. We will discuss the proposed merits these emerging agents bring to the treatment arsenal and how they compare with anti-VEGFs with regards to therapeutic activity, potency, specificity and safety. This review will also highlight recent pre-clinical research findings and suggest where future research might be directed.

PMID: 21170513 [PubMed - as supplied by publisher]

Clin Exp Optom. 2010 Dec 22. doi: 10.1111/j.1444-0938.2010.00553.x. [Epub ahead of print]

Drug delivery to the posterior segment of the eye through hydrogel contact lenses.

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Purpose: Despite pharmacological advances, delivery of drugs to the posterior segment of the eye remains problematic. We investigated the ability of hydrogel contact lenses to deliver small-molecule steroids, as well as larger biological molecules to the posterior segment.

Methods: Release characteristics of steroid-instilled lenses were studied in vitro. Drug delivery to the posterior segment of the eye was evaluated in a rabbit model, in which hydrogel contact lenses treated with diluted steroids (prednisolone or beclomethasone) were placed on rabbit corneas for four hours on days 1, 2, 5, 8 and 10. The amount of drug in plasma, posterior segment tissue and vitreous humour was measured with high-performance liquid chromatography-tandem mass spectrometry. In a further preliminary investigation, two rabbits were treated with ranibizumab.

Results: The lenses released prednisolone and beclomethasone in saline over a six-hour period at a declining rate. Prednisolone was found in posterior segment tissue from six of six rabbits at concentrations ranging from 26.8 to 166 ng/g and in vitreous humour from two of six rabbits. Beclomethasone was detected in posterior segment tissue from three rabbits but was not found in the vitreous humour. Ranibizumab was detected in posterior segment tissue in a range from 0.19 ng/mL to 0.5183 ng/mL.

Conclusions: Hydrogel contact lenses are a non-invasive, periocular drug delivery device capable of achieving measurable drug levels in posterior segment tissue.

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Genetics

Clin Chem Lab Med. 2010 Dec 23. [Epub ahead of print]

Review: Age-related macular degeneration: genetic and clinical findings.

Kokotas H, Grigoriadou M, Petersen MB.

Department of Genetics, Institute of Child Health, 'Aghia Sophia' Children's Hospital, Athens, Greece.

Abstract : Age-related macular degeneration (AMD) is a sight threatening eye disease that affects millions of humans over the age of 65 years. It is considered to be the major cause of irreversible blindness in the

elderly population in the developed world. The disease is prevalent in Europe and the United States, which has a large number of individuals of European descent. AMD is characterized by a progressive loss of central vision attributable to degenerative and neovascular changes that occur in the interface between the neural retina and the underlying choroid. This location contains the retinal photoreceptors, the retinal pigmented epithelium, a basement membrane complex known as Bruch's membrane and a network of choroidal capillaries. AMD is increasingly recognized as a complex genetic disorder where one or more genes contribute to an individual's susceptibility to development of the condition, while the prevailing view is that the disease stems from the interaction of multiple genetic and environmental factors. Although it has been proposed that a threshold event occurs during normal aging, the sequelae of biochemical, cellular, and molecular events leading to AMD are not fully understood. Here, we review the clinical aspects of AMD and summarize the genes which have been reported to have a positive association with the disease.

PMID: 21175380 [PubMed - as supplied by publisher]

Curr Eye Res. 2011 Jan;36(1):60-5.

Pigment epithelium-derived factor gene polymorphisms in exudative age-related degeneration in a Chinese cohort.

Qu Y, Zhang X, Dai H, Zhou F, Xu X, Zhang X, Bi H, Pan X, Wang H, Jiang H, Yin N, Dang G.

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Purpose: To investigate polymorphisms in the pigment epithelium-derived factor (PEDF) gene in a Chinese cohort with exudative age-related macular degeneration (AMD).

Methods: Two common single nucleotide polymorphisms (SNPs), Met72Thr (rs1136287) and -5736T>C (rs12150053), were genotyped, and four tagSNPs (tSNPs) were detected statistically in the PEDF gene of 168 exudative AMD patients and 230 age- and sex-matched control participants. Genetic analyses for additive, dominant, and recessive models were performed on all the available genotype data. All the possible haplotypes of these six SNPs were detected.

Results: No association was found between the patients and the control participants in the allele frequencies for any individual SNP. There was evidence to suggest that heterozygotes for rs1136287 (C/T) exerted a protective effect against exudative AMD (additive model, OR 0.59, CI 0.36-0.95, p?=?0.03), but none of the p-values in the other genotype groups were statistically significant. Likewise, haplotype analyses did not provide any evidence for an association between SNPs in the PEDF gene and the risk of exudative AMD in this Chinese cohort (p?>?0.05).

Conclusions: Detection of SNPs in the PEDF gene was not found to be significantly associated with exudative AMD in the Chinese cohort. Further studies of comprehensive PEDF gene variations are required to characterize the susceptibility of PEDF gene in the pathogenesis of AMD.

PMID: 21174599 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2010 Dec 17. [Epub ahead of print]

Dissection of Chromosome 16p12 Linkage Peak Suggests a Possible Role for CACNG3 Variants in Age-Related Macular Degeneration Susceptibility.

Spencer KL, Olson LM, Schnetz-Boutaud N, Gallins P, Wang G, Scott WK, Agarwal A, Jakobsdottir J, Conley Y, Weeks DE, Gorin MB, Pericak-Vance MA, Haines JL.

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Purpose: Age-related macular degeneration (AMD) is a complex disorder of the retina, characterized by drusen, geographic atrophy, and choroidal neovascularization. Cigarette smoking and the genetic variants CFH Y402H, ARMS2 A69S, CFB R32Q, and C3 R102G have been strongly and consistently associated

with AMD. Multiple linkage studies have found suggestive evidence of another AMD locus on chromosome 16p12, but the gene responsible has yet to be identified.

Methods: In the initial phase of our study, we tested single nucleotide polymorphisms (SNPs) across chromosome 16 for linkage and/or association in 575 Caucasian individuals from 148 multiplex and 77 singleton families. Additional variants were tested in an independent dataset of unrelated cases and controls, and using these results in combination with gene expression data and biological knowledge, we selected five genes for further study: CACNG3, HS3ST4, IL4R, Q7Z6F8, and ITGAM.

Results: After genotyping additional tagging SNPs across each gene, we found the strongest evidence for linkage and association within CACNG3, (rs757200 nonparametric LOD* 3.3, APL p=0.06, rs2238498 MQLS p=0.006 in the families, rs2283550 p=1.3x10(-6) and rs4787924 p=0.002 in the case-control dataset). After adjusting for known AMD risk factors, rs2283550 remained strongly associated (p=2.4x10(-4)). Furthermore, the association signal at rs4787924 was replicated in an independent dataset (p=0.035), and a joint analysis of all our data (p=0.001).

Conclusions: These results suggest that CACNG3 is the best candidate for an AMD risk gene within the 16p12 linkage peak. Future studies are needed to confirm this association and clarify the role of this gene in AMD pathogenesis.

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Pathogenesis & epidemiology

Graefes Arch Clin Exp Ophthalmol. 2010 Dec 21. [Epub ahead of print]

Association between asymmetry in cataract and asymmetry in age-related macular degeneration. The Beijing Eye Study.

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BACKGROUND: To examine in an intra-individual comparison whether cataract is associated with age-related macular degeneration (AMD).

METHODS: The population-based Beijing Eye Study included 4,439 subjects (age: 40+ years) out of 5,324 subjects invited to be examined. Using lens and fundus photographs, the amount of AMD was graded according to the Wisconsin Age-Related Maculopathy Grading system and the degree of cataract was graded using the system of the Age-Related Eye Disease Study.

RESULTS: Photographs with sufficient quality for bilateral examination of the lens and macula were available for 3,826 (86.2%) participants with a mean age of 55.3?±?10.0 years (range: 40-90 years) and a mean refractive error of -0.38?±?2.18 diopters (range: -20.13 diopters to +7.50 diopters). The side difference in presence of early AMD and late AMD respectively was not significantly associated with the inter-eye difference in the amount of nuclear cataract [P?=?0.27 and P?=?0.28 (r?=?0.02) respectively), amount of cortical cataract (P?=?0.12 and P?=?0.05 respectively), and amount of subcapsular posterior cataract (P?=?0.91 and P?=?0.85 respectively). In a similar manner, the side difference in the presence of early AMD and late AMD was not significantly associated with the inter-eye difference in the presence of nuclear cataract (P?=?0.99 and P?=?0.99 respectively), cortical cataract (P?=?0.25 and P?=?1.00 respectively), and subcapsular posterior cataract (P?=?0.59 and P?=?0.05 respectively). The side difference in the number of macular drusen was not significantly associated with the inter-eye difference in the amount of nuclear cataract (P?=?0.74), amount of cortical cataract (P?=?0.19) and amount of subcapsular posterior cataract (P?=?0.88). As a corollary, unilateral pseudophakia or aphakia was not significantly associated with inter-eye differences in the count (P?=?0.59) of drusen, and overall presence of early AMD (P?=?0.99) or late AMD (P?=?0.99).

CONCLUSIONS: In an intra-individual, inter-eye comparison, avoiding interdependencies of systemic

parameters, inter-eye difference was not significantly associated with any characteristics of age-related macular degeneration in either any type of cataract or in pseudophakia. This suggests that the development of cataract or cataract surgery did not markedly influence the development of age-related macular degeneration.

PMID: 21174115 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2010 Dec 17. [Epub ahead of print]

Are Lung Disease and Function Related to Age-Related Macular Degeneration?

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PURPOSE: To describe the relationship of lung disease and function with early age-related macular degeneration (AMD) in a population-based study.

DESIGN: A population-based, cross-sectional study of 12 596 middle-aged participants from the Atherosclerosis Risk in Communities Study.

METHODS: Lung function was assessed by spirometry. Physician diagnosis of asthma and lung disease was ascertained from a standardized questionnaire. AMD signs were graded from fundus photographs according to the Wisconsin grading protocol.

RESULTS: Among the study population, 587 (4.7%) had early AMD, 638 (5.1%) had asthma, and 581 (4.6%) had lung disease. After adjusting for age, gender, smoking, and hypertension, each 1-L increase in predicted forced expiratory volume in 1 second (odds ratio [OR], 1.27; 95% confidence interval [CI], 0.89 to 1.80), forced vital capacity (OR, 1.18; 95% CI, 0.93 to 1.51), and peak expiratory flow rate (OR, 1.12; 95% CI, 0.95 to 1.33) were not significantly associated with early AMD. Forced expiratory volume in 1 second-to-forced vital capacity ratio (second quartile OR, 1.61; 95% CI, 0.88 to 2.93, third quartile OR, 1.65; 95% CI 0.90 to 3.03; fourth quartile OR, 1.28; 95% CI 0.68 to 2.40) was not associated significantly with early AMD. Similarly, asthma (OR, 1.06; 95% CI, 0.86 to 1.27) and other lung diseases (OR, 1.08; 95% CI, 0.90 to 1.29) were not associated with early AMD.

CONCLUSIONS: Our data do not support a cross-sectional association between lung disease and risk of early AMD.

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Compositional studies of human RPE lipofuscin: mechanisms of molecular modifications.

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Abstract

The accumulation of lipofuscin has previously been implicated in several retinal diseases including Best's macular dystrophy, Stargardt's disease and age-related macular degeneration (AMD). Previously one of the major fluorophores of lipofuscin was identified as a bis-retinoid pyridinium salt called A2E, which is known to photochemically cause damage. In addition to A2E, there are numerous components in RPE lipofuscin that are unidentified. These compounds were determined to be structurally related to A2E by their fragmentation pattern with losses of 106, 190, 174 and/or 150 amu from the parent ion and the formation of fragments of ca 592 amu. The vast majority consists of relatively hydrophobic components corresponding to derivatized A2E with molecular weights in discrete groups of 800-900, 970-1080 and > 1200 m/z regions.

In order to determine the mechanism of these modifications, A2E was chemically modified by; (1) the formation of specific esters, (2) reaction with specific aldehydes and (3) spontaneous auto-oxidation. The contribution of ester formation to the naturally occurring components of lipofuscin was discounted since their fragmentation patterns were different to those found in vivo. Alternatively, reactions with specific aldehydes result in nearly identical products as those found in vivo. Artificial aging of RPE lipofuscin gives a complex mixture of structurally related components. This results from the auto- and/or photooxidation of A2E to form aldehydes, which then back react with A2E giving a series of higher molecular weight products. The majority of these modifications result in compounds that are much more hydrophobic than A2E. These higher molecular weight materials have increased values of log P compared to A2E. This increase in hydrophobicity most likely aids in the sequestering of A2E into granules with the concomitant diminution of its reactivity. Therefore, these processes may serve as protective mechanisms for the RPE.

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Over expressed or intraperitoneally injected human transferrin prevents photoreceptor degeneration in rd10 mice.

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PURPOSE: Retinal degeneration has been associated with iron accumulation in age-related macular degeneration (AMD), and in several rodent models that had one or several iron regulating protein impairments. We investigated the iron concentration and the protective role of human transferrin (hTf) in rd10 mice, a model of retinal degeneration.

METHODS: The proton-induced X-ray emission (PIXE) method was used to quantify iron in rd10 mice 2, 3, and 4 weeks after birth. We generated mice with the ß-phosphodiesterase mutation and hTf expression by crossbreeding rd10 mice with TghTf mice (rd10/hTf mice). The photoreceptor loss and apoptosis were evaluated by terminal deoxynucleotidyl transferase dUTP nick end labeling in 3-week-old rd10/hTf mice and compared with 3-week-old rd10 mice. The neuroprotective effect of hTf was analyzed in 5-day-old rd10 mice treated by intraperitoneal administration with hTf for up to 25 days. The retinal hTf concentrations and the thickness of the outer nuclear layer were quantified in all treated mice at 25 days postnatally.

RESULTS: PIXE analysis demonstrated an age-dependent iron accumulation in the photoreceptors of rd10 mice. The rd10/hTf mice had the rd10 mutation, expressed high levels of hTf, and showed a significant decrease in photoreceptor death. In addition, rd10 mice intraperitoneally treated with hTf resulted in the retinal presence of hTf and a dose-dependent reduction in photoreceptor degeneration.

CONCLUSIONS: Our results suggest that iron accumulation in the retinas of rd10 mutant mice is associated with photoreceptor degeneration. For the first time, the enhanced survival of cones and rods in the retina of this model has been demonstrated through overexpression or systemic administration of hTf. This study highlights the therapeutic potential of Tf to inhibit iron-induced photoreceptor cell death observed in degenerative diseases such as retinitis pigmentosa and age-related macular degeneration.

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