

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

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

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

Drug treatment

Arch Ophthalmol. 2012 Feb;130(2):190-194.

Evaluation of Masking Study Participants to Intravitreal Injections in a Randomized Clinical Trial.

Glassman AR, Stockdale CR, Beck RW, Baker C, Bressler NM; for the Diabetic Retinopathy Clinical Research Network.

Jaeb Center for Health Research, 15310 Amberly Dr, Ste 350, Tampa, FL 33647. drcrstat2@jaeb.org.

OBJECTIVE: To evaluate the success of masking study participants to treatment allocation using sham intravitreal injections.

METHODS: Eyes were randomized to receive sham injections plus prompt laser, intravitreal ranibizumab injections plus prompt laser, intravitreal ranibizumab injections plus deferred laser, or intravitreal triamcinolone acetonide injections plus prompt laser up to every 16 weeks with sham injections intermittently. All eyes could receive treatment or sham as often as every 4 weeks. Participants with 2 study eyes had 1 eye randomized to sham plus prompt laser and 1 eye randomized to a real injection group. Sham injections were performed by pressing the syringe hub against the conjunctiva to mimic a real injection. Laser treatment was not masked. At the 1-year visit, participants were asked if they believed that the injections received during the study were real, sham, or sometimes real and sometimes sham.

RESULTS: Among 423 participants with 1 study eye, the correct assignment was stated by 9.9% of the sham plus prompt laser group, 88.0% of the ranibizumab plus prompt laser group, 89.6% of the unmasked ranibizumab plus deferred laser group, and 44.0% of the triamcinolone plus prompt laser group. Among 112 participants with 2 study eyes, the correct assignment was stated for 24.1% of the sham plus prompt laser eyes.

CONCLUSIONS: Successful masking of an intravitreal injection can be accomplished when a sham injection procedure carefully mimics a real injection procedure. Masking seems less successful when one eye is receiving a real injection and the other eye is receiving a sham injection or when an individual eye receives both real and sham injections.

PMID: 22332211 [PubMed - as supplied by publisher]

Ophthalmology. 2012 Feb 11. [Epub ahead of print]

Ranibizumab for Diabetic Macular Edema: Results from 2 Phase III Randomized Trials: RISE and RIDE.

Nguyen QD, Brown DM, Marcus DM, Boyer DS, Patel S, Feiner L, Gibson A, Sy J, Rundle AC, Hopkins JJ, Rubio RG, Ehrlich JS; RISE and RIDE Research Group(□).

Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland.

PURPOSE: To evaluate the efficacy and safety of intravitreal ranibizumab in diabetic macular edema (DME) patients.

DESIGN: Two parallel, methodologically identical, phase III, multicenter, double-masked, sham injection-controlled, randomized studies.

PARTICIPANTS: Adults with vision loss from DME (best-corrected visual acuity [BCVA], 20/40-20/320 Snellen equivalent) and central subfield thickness ≥ 275 μ m on time-domain optical coherence tomography (OCT).

INTERVENTION: Monthly intravitreal ranibizumab (0.5 or 0.3 mg) or sham injections. Macular laser was available per-protocol-specified criteria.

MAIN OUTCOME MEASURES: Proportion of patients gaining ≥ 15 letters in BCVA from baseline at 24 months.

RESULTS: In RISE (NCT00473330), 377 patients were randomized (127 to sham, 125 to 0.3 mg, 125 to 0.5 mg). At 24 months, 18.1% of sham patients gained ≥ 15 letters versus 44.8% of 0.3-mg ($P < 0.0001$; difference vs sham adjusted for randomization stratification factors, 24.3%; 95% confidence interval [CI], 13.8-34.8) and 39.2% of 0.5-mg ranibizumab patients ($P < 0.001$; adjusted difference, 20.9%; 95% CI, 10.7-31.1). In RIDE (NCT00473382), 382 patients were randomized (130 to sham, 125 to 0.3 mg, 127 to 0.5 mg). Significantly more ranibizumab-treated patients gained ≥ 15 letters: 12.3% of sham patients versus 33.6% of 0.3-mg patients ($P < 0.0001$; adjusted difference, 20.8%; 95% CI, 11.4-30.2) and 45.7% of 0.5-mg ranibizumab patients ($P < 0.0001$; adjusted difference, 33.3%; 95% CI, 23.8-42.8). Significant improvements in macular edema were noted on OCT, and retinopathy was less likely to worsen and more likely to improve in ranibizumab-treated patients. Ranibizumab-treated patients underwent significantly fewer macular laser procedures (mean of 1.8 and 1.6 laser procedures over 24 months in the sham groups vs 0.3-0.8 in ranibizumab groups). Ocular safety was consistent with prior ranibizumab studies; endophthalmitis occurred in 4 ranibizumab patients. The total incidence of deaths from vascular or unknown causes, nonfatal myocardial infarctions, and nonfatal cerebrovascular accidents, which are possible effects from systemic vascular endothelial growth factor inhibition, was 4.9% to 5.5% of sham patients and 2.4% to 8.8% of ranibizumab patients.

CONCLUSIONS: Ranibizumab rapidly and sustainably improved vision, reduced the risk of further vision loss, and improved macular edema in patients with DME, with low rates of ocular and nonocular harm.

PMID: 22330964 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Can J Ophthalmol. 2012 Feb;47(1):62-5.

Scotoma displacement in the macular mapping test as a tool for identification of preferred retinal loci.

Al-Serafi M, Markowitz SN, Reyes SV.

Low Vision Service (University Health Network Hospitals), Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ont.

OBJECTIVE: To clarify the efficacy of the macular mapping test (MMT) to identify eccentric fixation with preferred retinal loci (PRL).

DESIGN: Retrospective observational case series from archived data.

PARTICIPANTS: Cases with age-related macular degeneration with low vision in both eyes and best corrected visual activity (BCVA) of 20/50 to 20/400 in the better eye.

METHODS: Identification of preferred retinal loci with the Nidek MP-1 microperimeter and correlation with scotoma displacement on perimetry records as recorded with the MMT.

RESULTS: We recruited data on 43 patients (12 males and 31 females), aged 57-96 years (mean 84.05 years $\pm$ SD 8.00). Mean BCVA was 0.9 ± 0.32 SD logMar units (20/160). PRL location matched the direction of scotoma displacement in 32 study subjects (74.41%, $p < 0.002$).

CONCLUSIONS: Scotoma displacement recorded with the MMT offers reasonable indirect estimates on PRL location.

PMID: 22333854 [PubMed - in process]

Can J Ophthalmol. 2012 Feb;47(1):24-7.

Ultrasound biomicroscopy study of vitreous incarceration subsequent to intravitreal injections.

Hodjatjalali K, Riazi M, Faghihi H, Khorami A.

Noor Ophthalmology Research Center, Noor Eye Hospital, Tehran, Iran.

OBJECTIVE: To study the existence of vitreous incarceration by ultrasound biomicroscopy (UBM) at the pars plana after direct intravitreal injection of triamcinolone acetonide $\pm$ bevacizumab without anterior chamber paracentesis.

DESIGN: Interventional case series.

PARTICIPANTS: Patients undergoing intravitreal injection of triamcinolone acetonide with or without intravitreal bevacizumab.

METHODS: In 21 eyes, the existence of vitreous incarceration at the pars plana site of intravitreal injection of 0.05 mL of drug was studied by UBM (50 MHz probe of the VUmax, Sonomed, NY), the day after surgery, by 1 technician. The reason for injection was diabetic retinopathy in 12 (57.1%) eyes; age-related macular degeneration in 6 (28.6%) eyes; branch retinal vein occlusion in 2 (9.5%) eyes; and choroiditis in 1 eye (4.8%). In 1 eye, only triamcinolone acetonide was injected, and in the other eyes, bevacizumab mixed with triamcinolone acetonide was injected.

RESULTS: We studied 21 eyes in 13 patients. Of the subjects, 61.5% were male. The mean age of the patients was 62.2 years. On the day after intravitreal injection of the drug, vitreous incarceration into the pars plana site was detected by UBM in 42.9% of the eyes.

CONCLUSION: Vitreous incarceration exists after intravitreal injection of drug, but its clinical importance is still unknown. Further long-term prospective studies are recommended.

PMID: 22333847 [PubMed - in process]

Pathogenesis

Mol Neurodegener. 2012 Feb 10;7(1):7. [Epub ahead of print]

Rapid glutamate receptor 2 trafficking during retinal degeneration.

Lin Y, Jones BW, Liu A, Vazquez-Chona FR, Lauritzen JS, Ferrell WD, Marc RE.

BACKGROUND: Retinal degenerations, such as age-related macular degeneration (AMD) and retinitis pigmentosa (RP), are characterized by photoreceptor loss and anomalous remodeling of the surviving retina that corrupts visual processing and poses a barrier to late-stage therapeutic interventions in particular. However, the molecular events associated with retinal remodeling remain largely unknown. Given our prior evidence of ionotropic glutamate receptor (iGluR) reprogramming in retinal degenerations, we hypothesized that the edited glutamate receptor 2 (GluR2) subunit and its trafficking may be modulated in retinal degenerations.

RESULTS: Adult albino Balb/C mice were exposed to intense light for 24 h to induce light-induced retinal degeneration (LIRD). We found that prior to the onset of photoreceptor loss, protein levels of GluR2 and related trafficking proteins, including glutamate receptor-interacting protein 1 (GRIP1) and postsynaptic density protein 95 (PSD-95), were rapidly increased. LIRD triggered neuritogenesis in photoreceptor survival regions, where GluR2 and its trafficking proteins were expressed in the anomalous dendrites. Immunoprecipitation analysis showed interaction between KIF3A and GRIP1 as well as PSD-95, suggesting that KIF3A may mediate transport of GluR2 and its trafficking proteins to the novel dendrites. However, in areas of photoreceptor loss, GluR2 along with its trafficking proteins nearly vanished in retracted retinal neurites.

CONCLUSIONS: All together, LIRD rapidly triggers GluR2 plasticity, which is a potential mechanism behind functionally phenotypic revisions of retinal neurons and neuritogenesis during retinal degenerations.

PMID: 22325330 [PubMed - as supplied by publisher]

Epidemiology

Br J Ophthalmol. 2012 Feb 13. [Epub ahead of print]

The estimated prevalence and incidence of late stage age related macular degeneration in the UK.

Owen CG, Jarrar Z, Wormald R, Cook DG, Fletcher AE, Rudnicka AR.

St George's, University of London, London, UK.

Background: UK estimates of age related macular degeneration (AMD) occurrence vary.

Aims: To estimate prevalence, number and incidence of AMD by type in the UK population aged ≥50 years.

Methods: Age-specific prevalence rates of AMD obtained from a Bayesian meta-analysis of AMD prevalence were applied to UK 2007-2009 population data. Incidence was estimated from modelled age-specific prevalence.

Results: Overall prevalence of late AMD was 2.4% (95% credible interval (CrI) 1.7% to 3.3%), equivalent to 513 000 cases (95% CrI 363 000 to 699 000); estimated to increase to 679 000 cases by 2020. Prevalences were 4.8% aged ≥65 years, 12.2% aged ≥80 years. Geographical atrophy (GA) prevalence rates were 1.3% (95% CrI 0.9% to 1.9%), 2.6% (95% CrI 1.8% to 3.7%) and 6.7% (95% CrI 4.6% to 9.6%); neovascular AMD (NVAMD) 1.2% (95% CrI 0.9% to 1.7%), 2.5% (95% CrI 1.8% to 3.4%) and 6.3% (95% CrI 4.5% to 8.6%), respectively. The estimated number of prevalent cases of late AMD were 60% higher in women versus men (314 000 cases in women, 192 000 men). Annual incidence of late AMD, GA and NVAMD per 1000 women was 4.1 (95% CrI 2.4% to 6.8%), 2.4 (95% CrI 1.5% to 3.9%) and 2.3 (95% CrI 1.4% to 4.0%); in men 2.6 (95% CrI 1.5% to 4.4%), 1.7 (95% CrI 1.0% to 2.8%) and 1.4 (95% CrI 0.8% to 2.4%), respectively. 71 000 new cases of late AMD were estimated per year.

Conclusions: These estimates will guide health and social service provision for those with late AMD and enable estimation of the cost of introducing new treatments.

PMID: 22329913 [PubMed - as supplied by publisher]

Singapore Med J. 2012 Feb;53(2):82-7.

Review of key findings from the Singapore Malay Eye Study (SiMES-1).

Rosman M, Zheng Y, Lamoureux E, Saw SM, Aung T, Tay WT, Wang JJ, Mitchell P, Tai ES, Wong TY.

Singapore Eye Research Institute, 11 Third Hospital Ave, #05-00, Singapore 168751. ophwty@nus.edu.sg.

Introduction: This study highlights the key epidemiological findings from the Singapore Malay Eye Study (SiMES-1).

Methods: SiMES-1 was a cross-sectional, population-based epidemiological study on eye diseases. It was performed on 3,280 randomly selected Malay adults living in the south-western part of Singapore. All study participants underwent various validated questionnaires and detailed eye examinations. A review of all papers published from SiMES-1 was performed.

Results: A total of 24.6% of the study population had myopia, while 35.3% had hyperopia and 39.4% had astigmatism. 20.4% of the population had under-corrected refractive error. 1,338 (45.7%) participants were diagnosed to have cataracts in at least one eye. 8.6% of the study population had undergone cataract surgery in either eye, while 4.7% had bilateral cataract surgery. 150 (4.6%) participants were diagnosed to have glaucoma, of which primary open angle glaucoma was the most common type (3.2% of the study population), followed by secondary glaucoma (0.8%) and primary angle closure glaucoma (0.2%). Pterygium was diagnosed in 508 out of 3,266 study participants, giving a prevalence rate of 15.6%. The presence of diabetic retinopathy was observed in 421 (12.9%) out of 3,265 study participants. 183 (5.6%) study participants had some degree of age-related macular degeneration (AMD), of which 23 (0.7%) were classified as having late AMD.

Conclusion: This paper provides a summary of the prevalence of common eye diseases among the Singaporean adult Malay population and provides data useful for public health education and disease prevention.

PMID: 22337179 [PubMed - in process]

Genetics

Ocul Immunol Inflamm. 2012 Feb;20(1):27-36.

Genetics of Immunological and Inflammatory Components in Age-related Macular Degeneration.

Tuo J, Grob S, Zhang K, Chan CC.

Immunopathology Section, Laboratory of Immunology, National Eye Institute, National Institutes of Health , Bethesda , MD ;

Abstract

Age-related macular degeneration (AMD), affecting 30 to 50 million elder individuals worldwide, is a disease affecting the macular retina and choroid that can lead to irreversible central vision loss and blindness. Recent findings support a role for immunologic processes in AMD pathogenesis, including generation of inflammatory related molecules in the Bruch's membrane, recruitment of macrophages, complement activation, microglial activation and accumulation in the macular lesions. Pro-inflammatory effects of chronic inflammation and oxidative stress can result in abnormal retinal pigment epithelium, photoreceptor atrophy and choroidal neovascularization. The associations of immunological and inflammatory genes, in particular the genes related to innate immunity with AMD support the involvement of various immunological pathways in the AMD pathogenesis. We review the literature on the involvements of inflammatory genes in AMD, highlight recent genetic discoveries, and discuss the potential application of such knowledge in the management of patients with AMD.

PMID: 22324898 [PubMed - in process]

Am J Epidemiol. 2012 Feb 10. [Epub ahead of print]

Apolipoprotein E Gene Associations in Age-related Macular Degeneration: The Melbourne Collaborative Cohort Study.

Adams MK, Simpson JA, Richardson AJ, English DR, Aung KZ, Makeyeva GA, Guymer RH, Giles GG, Hopper J, Robman LD, Baird PN.

Abstract

The apolipoprotein E gene (APOE) has been found to be associated with age-related macular degeneration (AMD). Reported associations have been questioned, as they are opposite those for Alzheimer's disease and cardiovascular disease. The authors examined associations between APOE genotype and AMD using a case-control study (2,287 cases and 2,287 controls individually matched on age, sex, and country of origin) nested within Melbourne Collaborative Cohort Study participants aged 48-86 years at AMD detection. The odds ratio for early AMD among participants with $\epsilon 2$ -containing genotypes ($\epsilon 2\epsilon 2/\epsilon 2\epsilon 3/\epsilon 2\epsilon 4$) was 1.32 (95% confidence interval (CI): 1.11, 1.58; $P = 0.002$) versus persons with genotype $\epsilon 3\epsilon 3$. Associations with early AMD varied by smoking status; $\epsilon 2$ -containing genotypes were positively associated with early AMD for never and previous smokers (never smokers: odds ratio (OR) = 1.40, 95% CI: 1.12, 1.76 ($P = 0.003$); previous smokers: OR = 1.39, 95% CI: 1.00, 1.93 ($P = 0.05$)) but not for current smokers (OR = 0.66, 95% CI: 0.34, 1.30 ($P = 0.2$; interaction $P = 0.05$). The $\epsilon 4$ -containing genotype group ($\epsilon 3\epsilon 4/\epsilon 4\epsilon 4$) had an inverse association with early AMD among current smokers only (OR = 0.41, 95% CI: 0.22, 0.77 ($P = 0.005$)). These results highlight the importance of stratifying by smoking status in elderly populations. Smokers who survive to old age may be more likely to possess unknown genotypes which modify exposure-disease associations.

PMID: 22328704 [PubMed - as supplied by publisher]

Mol Biol Rep. 2012 Feb 14. [Epub ahead of print]

Genetic polymorphism of the iron-regulatory protein-1 and -2 genes in age-related macular degeneration.

Synowiec E, Pogorzelska M, Blasiak J, Szaflik J, Szaflik JP.

Department of Molecular Genetics, University of Lodz, Pomorska 141/143, 90-236, Lodz, Poland.

Abstract

Iron can be involved in the pathogenesis of AMD through the oxidative stress because it may catalyze the Haber-Weiss and Fenton reactions converting hydrogen peroxide to free radicals, which can induce cellular damage. We hypothesized that genetic polymorphism in genes related to iron metabolism may predispose individuals to the development of AMD and therefore we checked for an association between the g.32373708 G>A polymorphism (rs867469) of the IRP1 gene and the g.49520870 G>A (rs17483548) polymorphism of the IRP2 gene and AMD risk as well as the modulation of this association by some environmental and life-style factors. Genotypes were determined in DNA from blood of 269 AMD patients and 116 controls by the allele-specific oligonucleotide-restriction fragment length polymorphism and the polymerase chain reaction-restriction fragment length polymorphism. An association between AMD, dry and wet forms of AMD and the G/G genotype of the g.32373708 G>A-IRP1 polymorphism was found (OR 3.40, 4.15, and 2.75). On the other hand, the G/A genotype reduced the risk of AMD as well as its dry or wet form (OR 0.23, 0.21, 0.26). Moreover, the G allele of the g.49520870 G>A-IRP2 polymorphism increased the risk of the dry form of the disease (OR 1.51) and the A/A genotype and the A allele decreased such risk (OR 0.43 and 0.66). Our data suggest that the g.32373708 G>A-IRP1 and g.49520870 G>A-IRP2 polymorphisms may be associated with increased risk for AMD.

PMID: 22331484 [PubMed - as supplied by publisher]

Diet

Ophthalmology. 2012 Feb 11. [Epub ahead of print]

Yellow Corneal Ring Associated with Vitamin Supplementation for Age-Related Macular Degeneration.

Eller AW, Gorovoy IR, Mayercik VA.

Retina Service, UPMC Eye Center, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.

PURPOSE: To report the first described cases of peripheral yellow corneal rings secondary to vitamin supplementation for age-related macular degeneration (ARMD).

DESIGN: Retrospective single-center case series.

PARTICIPANTS: The eyes of 4 patients taking vitamin supplementation for ARMD were examined at the University of Pittsburgh Medical Center Department of Ophthalmology between January 2010 and April 2011.

METHODS: We reviewed the medical records of 4 patients with peripheral corneal rings receiving vitamin supplementation for ARMD.

MAIN OUTCOME MEASURES: The presence of peripheral yellow corneal rings, skin findings, and serum carotene levels.

RESULTS: Each patient had circumferential, yellow, peripheral corneal rings and exhibited subtle yellowing of the skin most notable on the palms. Serum carotene levels were normal in 2 of the 3 patients and markedly elevated in the last patient in whom it was measured.

CONCLUSIONS: It is unclear at this time how to counsel patients with this ocular finding. We suspect that these rings are more common than generally appreciated because they may have a subtle appearance or be misdiagnosed as arcus senilis. We suggest that a formal study be performed on a cohort of patients taking vitamin supplementation for macular degeneration that specifically screens for yellow rings and measures serum carotene levels when they are identified.

PMID: 22330962 [PubMed - as supplied by publisher]

Arch Ophthalmol. 2012 Feb;130(2):254-5.

Use of micronutrient supplement for preventing advanced age-related macular degeneration in Japan.

Sasaki M, Shinoda H, Koto T, Uchida A, Tsubota K, Ozawa Y.

Department of Ophthalmology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan. ozawa@a5.keio.jp.

PMID: 22332227 [PubMed - in process]

Disclaimer: This newsletter is provided as a free service to eye care professionals by the Macular Degeneration Foundation. The Macular Degeneration Foundation cannot be liable for any error or omission in this publication and makes no warranty of any kind, either expressed or implied in relation to this publication.