Retina Roundup

March 2022

1.Opthalmology Retina : **REPORT**| VOLUME 6, ISSUE 2, P181-182, FEBRUARY 01, 2022

Dexamethasone Eye Drops for the Treatment of Retinopathy of Prematurity

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Published:September 10, 2021

DOI:https://doi.org/10.1016/j.oret.2021.09.002

Hyperlink : https://www.ophthalmologyretina.org/article/S2468-6530(21)00285-2/fulltext

2. Am J Ophthalmol 2022 Feb;234:59-70.

Cognitive Outcomes Following Intravitreal Bevacizumab for Retinopathy of Prematurity: 4- to 6-Year Outcomes in a Prospective Cohort

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Abstract

Purpose: To determine the long-term cognitive outcomes in children who underwent intravitreal bevacizumab (IVB) for retinopathy of prematurity (ROP).

Design: Prospective cohort study.

Methods: This single-center study enrolled 186 children between 3 and 6 years of age and included 101 children in the final analysis: premature without ROP (group 1), ROP not needing treatment (group 2), IVB monotherapy (group 3), IVB plus laser therapy (group 4), and laser monotherapy (group 5). The Full-Scale Intelligence Quotient (FSIQ) was evaluated by the Wechsler Preschool and Primary Scale of Intelligence Test at baseline and then annually for 1-2 years and compared among groups.

Results: The age at cognitive evaluation was 4.5-4.9 years at baseline and 6.1-7.0 years at the last follow-up. The FSIQ was comparable among the groups at both time points (P = .08 and .50, respectively). Severe cognitive impairment (FSIQ < 70) was more common in group 4 at baseline (4%, 22%, 13%, 33%, and 0% in groups 1-5, respectively; P = .03) but did not differ among the groups at the last follow-up (6%, 0%, 4%, 22%, and 0%; P = .22). After adjusting for sex, Apgar score, neonatal adverse events, and days on mechanical ventilation, IVB was not associated with FSIQ either at baseline or at the last follow-up.

Conclusions: At 4.5 to beyond 6 years of age, children who underwent IVB monotherapy had comparable cognitive outcomes compared to the other premature

children without prior IVB. Children who underwent IVB plus laser showed higher severe cognitive impairment at 4.5 years of age.

DOI: 10.1016/j.ajo.2021.06.034

3. Ophthalmology, 2022 Feb 8;S0161-6420(22)00090-2.

Photoreceptor layer thinning is an early biomarker for age-related macular degeneration: Epidemiological and genetic evidence from UK Biobank optical coherence tomography data

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Abstract

Objective: Despite widespread use of optical coherence tomography (OCT), an early-stage imaging biomarker for age-related macular degeneration (AMD) has not been identified. Pathophysiologically, the timing of drusen accumulation in relation to photoreceptor degeneration in AMD remains unclear, as are the inherited genetic variants contributing to these processes. Here, we jointly analyzed OCT, electronic health record, and genomic data to characterize the time sequence of changes in retinal layer thicknesses in AMD, as well as epidemiological and genetic associations between retinal layer thicknesses and AMD.

Design: Cohort study PARTICIPANTS: 44,823 UK Biobank individuals (enrollment ages 40-70y, 54% female, median 10y follow-up).

Methods: The Topcon Advanced Boundary Segmentation algorithm was used for retinal layer segmentation. We associated 9 retinal layer thicknesses with prevalent AMD (present at enrollment) in a logistic regression model, and with incident AMD (diagnosed after enrollment) in a Cox proportional hazards model. Next, we associated AMD-associated genetic alleles, individually and as a polygenic risk score (PRS), with retinal layer thicknesses. All analyses were adjusted for age, age^2, sex, smoking status, and principal components of ancestry.

Main outcome measures: Prevalent and incident AMD RESULTS: Photoreceptor segment (PS) thinning was observed throughout the lifespan of individuals analyzed, while retinal pigment epithelium and Bruch's membrane complex (RPE+BM) thickening started after age 57y. Each standard deviation (SD) of PS thinning and RPE+BM thickening were associated with incident AMD (PS: HR 1.35, 95% CI 1.23-1.47, P=3.7x10^{-11}; RPE+BM: HR 1.14, 95% CI 1.06-1.22, P=0.00024). The AMD PRS was associated with PS thinning (Beta -0.21 SD per 2-fold genetically increased risk of AMD, 95% CI -0.23 to -0.19, P=2.8x10^{-74}), and its association with RPE+BM was U-shaped (thinning with AMD PRS<92nd percentile and thickening with AMD

PRS>92nd percentile). The loci with strongest support for genetic correlation were AMD risk-raising variants CFH:rs570618-T, CFH:10922109-C, and ARMS2/HTRA1:rs3750846-C on PS thinning, and SYN3/TIMP3:rs5754227-T on RPE+BM thickening.

Conclusions: Epidemiologically, PS thinning precedes RPE+BM thickening by decades, and is the retinal layer most strongly predictive of future AMD risk. Genetically, AMD risk variants are associated with decreased PS thickness. Overall, these findings support PS thinning as an early-stage biomarker for future AMD development.

DOI: 10.1016/j.ophtha.2022.02.001

4. Front Neurosci. 2021; 15: 780841. Published online 2022 Jan 10.

Blocking Ocular Sympathetic Activity Inhibits Choroidal Neovascularization

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Abstract :

Purpose: To investigate how modulating ocular sympathetic activity affects progression of choroidal neovascularization (CNV), a hallmark feature of wet age-related macular degeneration (AMD).

Methods: In the first of two studies, Brown Norway rats underwent laser-induced CNV and were assigned to one of the following groups: daily eye drops of artificial tears (*n* = 10; control group); daily eye drops of the β-adrenoreceptor agonist isoproterenol (*n* = 10); daily eye drops of the β-adrenoreceptor antagonist propranolol (*n* = 10); sympathetic internal carotid nerve (ICN) transection 6 weeks prior to laser-induced CNV (*n* = 10). In the second study, rats underwent laser-induced CNV followed by ICN transection at different time points: immediately after the laser injury (*n* = 6), 7 days after the laser injury (*n* = 6), and sham surgery 7 days after the laser injury (*n* = 6; control group). All animals were euthanized 14 days after laser application. CNV development was quantified with fluorescein angiography and optical coherence tomography (*in vivo*), as well as lesion volume analysis using 3D confocal reconstruction (postmortem). Angiogenic growth factor protein levels in the choroid were measured with ELISA.

Results: In the first study, blocking ocular sympathetic activity through pharmacological or surgical manipulation led to a 75% or 70% reduction in CNV lesion volume versus the control group, respectively ($P < 0.001$). Stimulating ocular sympathetic activity with isoproterenol also led to a reduction in lesion volume, but only by 27% versus controls ($P < 0.05$). VEGF protein levels in the choroid were

elevated in the three treatment groups ($P < 0.01$). In the second study, fluorescein angiography and CNV lesion volume analysis indicated that surgically removing the ocular sympathetic supply inhibited progression of laser-induced CNV, regardless of whether ICN transection was performed on the same day or 7 days after the laser injury.

Conclusion: Surgical and pharmacological block of ocular sympathetic activity can inhibit progression of CNV in a rat model. Therefore, electrical block of ICN activity could be a potential bioelectronic medicine strategy for treating wet AMD.

Keywords: wet AMD, internal carotid nerve, choroidal neovascularization, ocular sympathetic activity, laser-induced CNV, β-adrenoreceptor modulation

DOI: 10.3389/fnins.2021.780841

5. Ophthalmol Retina, 2022 Feb 1;S2468-6530(22)00041-0.

Prophylactic Ranibizumab to Prevent Neovascular Age-Related Macular Degeneration in Vulnerable Fellow Eyes: A Randomized Clinical Trial

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Abstract

Purpose: To determine whether prophylactic ranibizumab prevents the development of neovascular age-related macular degeneration (nAMD) in eyes with intermediate AMD for patients with pre-existing nAMD in their contralateral eye.

Design: Multicenter randomized clinical trial.

Participants: Adults aged 50 and older with intermediate AMD (multiple intermediate drusen [≥ 63 μm and <125 μm] or ≥1 large drusen [≥125 μm] and pigmentary changes) in the study eye and nAMD in the contralateral eye.

Intervention: Intravitreal ranibizumab injection (0.5 mg) every 3 months for 24 months or sham injection.

Main outcome measures: Conversion to nAMD over 24 months (primary). Change in best-corrected visual acuity from baseline to 24 months (secondary).

Results: Among 108 enrolled participants (54 [50%] in each group), all except two were non-Hispanic Whites, 61 participants (56%) were female, and the mean age was 78 years. The mean baseline visual acuity was 77.7 letters (Snellen equivalent 20/32). The rate of conversion to nAMD over 24 months was 7 of 54 eyes (13%) in both groups (ranibizumab vs. sham hazard ratio=0.91 [95% CI, 0.32-2.59], P=.86). At 24 months,

the cumulative incidence of nAMD adjusted for loss to follow-up was 14% (95% CI, 4%-23%) in the ranibizumab group and 15% (95% CI, 4%-25%) in the sham group. At 24 months, the mean change in visual acuity from baseline was -2.1 letters (standard deviation, 5.4) with ranibizumab and -1.4 letters (standard deviation, 7.7) with sham (adjusted difference=-0.8 [95% CI, -3.7 to 2.2], P=.63). The proportion of eyes that lost at least 10 letters of visual acuity from baseline at 24 months was 2 of 39 (5%) with ranibizumab and 4 of 40 (10%) with sham. There were no serious ocular adverse events in either group.

Conclusions: Quarterly dosing of 0.5 mg ranibizumab in eyes with intermediate AMD did not reduce the incidence of nAMD as compared to sham injections; however, the study was likely underpowered given the 95% confidence interval, and a clinically meaningful effect cannot be excluded. There also was no effect on visual acuity at 24 months. Other strategies to reduce neovascular conversion in these vulnerable eyes are needed.

Keywords: exudative age-related macular degeneration; geographic atrophy; intermediate age-related macular degeneration; neovascular age-related macular degeneration; nonexudative age-related macular degeneration; ranibizumab.

DOI: 10.1016/j.oret.2022.01.019