NEW RETINA ROUNDUP

January 2022

Dear Friends and Colleagues,

This January 2022 segment of the “New Retina Roundup” contains the compilation of a few interesting articles of the preceding month.

Visit https://youtu.be/0x3D66d2zz0 to watch the video of New Retina Roundup of January 2022

1. Retina. 2021 Oct 1;41(10):2163-2171. doi: 10.1097/IAE.0000000000003147.

A MULTIFACTORIAL APPROACH FOR IMPROVING THE SURGICAL PERFORMANCE OF NOVICE VITREORETINAL SURGEONS.

Roizenblatt M(1)(2)(3), Jiramongkolchai K(3), Gehlbach PL(3), Dias Gomes Barrios Marin V(1), Treiger Grupenmacher A(1), Muralha F(1), Eid Farah M(1)(2), Belfort Junior R(1)(2), Maia M(1)(2).

PURPOSE: To quantitatively analyze and compare the novice vitreoretinal surgeons' performance after various types of external exposures.

METHODS: This prospective, self-controlled, cross-sectional study included 15 vitreoretinal fellows with less than 2 years of experience. Surgical performance was assessed using the Eyesi simulator after each exposure: Day 1, placebo, 2.5, and 5 mg/kg caffeine; Day 2, placebo, 0.2, and 0.6 mg/kg propranolol; Day 3, baseline simulation, breathalyzer reading of 0.06% to 0.10% and 0.11% to 0.15% blood alcohol concentration; Day 4, baseline simulation, push-up sets with 50% and 85% repetition maximum; Day 5, 3-hour sleep deprivation. Eyesi-generated total scores were the main outcome measured (0-700, worst to best).

RESULTS: Performances worsened after increasing alcohol exposure based on the total score ($\chi 2 = 7$; degrees of freedom = 2; $P = 0.03$). Blood alcohol concentration 0.06% to 0.10% and 0.11% to 0.15% was associated with diminished performance compared with improvements after propranolol 0.6 and 0.2 mg/kg, respectively ($\Delta 1 = -22$ vs. $\Delta 2 = +13$; $P = 0.02$; $\Delta 1 = -43$ vs. $\Delta 2 = +23$; $P = 0.01$). Propranolol 0.6 mg/kg was positively associated with the total score, compared with deterioration after 2.5 mg/kg caffeine ($\Delta 1 = +7$ vs. $\Delta 2 = -13$; $P = 0.03$).

CONCLUSION: Surgical performance diminished dose dependently after alcohol. Caffeine 2.5 mg/kg was negatively associated with dexterity, and performance improved after 0.2 mg/kg propranolol. No changes occurred after short-term exercise or acute 3-hour sleep deprivation.

DOI: 10.1097/IAE.0000000000003147
PMID: 34543245 [Indexed for MEDLINE]

2. JAMA Ophthalmol. 2021 Dec 1;139(12):1266-1273. doi: 10.1001/jamaophthalmol.2021.4103.

LAPSES IN CARE AMONG PATIENTS ASSIGNED TO RANIBIZUMAB FOR PROLIFERATIVE DIABETIC RETINOPATHY: A POST HOC ANALYSIS OF A RANDOMIZED CLINICAL TRIAL.

Maguire MG(1), Liu D(2), Bressler SB(3), Friedman SM(4), Melia M(2), Stockdale CR(2), Glassman AR(2), Sun JK(5)(6); DRCR Retina Network.

IMPORTANCE: The follow-up schedule for individuals with eyes treated with anti-vascular endothelial growth factor agents for proliferative diabetic retinopathy (PDR) requires that patients return frequently for monitoring and repeated treatment. The likelihood that a patient will comply should be a consideration in choosing a treatment approach.

OBJECTIVE: To describe completion of scheduled examinations among participants assigned to intravitreous injections of ranibizumab for PDR in a multicenter randomized clinical trial.

DESIGN, SETTING, AND PARTICIPANTS: This post hoc analysis evaluates data from a randomized clinical trial conducted at 55 US sites among 305 adults with proliferative diabetic retinopathy enrolled between February and December 2012.

MAIN OUTCOMES AND MEASURES: A long lapse in care of 8 or more weeks past a scheduled examination, dropout from follow-up, visual acuity at 5 years.

RESULTS: Among 170 participants, the median age was 51 years, and 44.7% were female. Through 5 years of follow-up, 94 of 170 participants (55.3%) had 1 or
more long lapse in care. Median time to the first long lapse was 210 weeks, and 69 of 94 participants (73.4%) returned for examination after the first long lapse. Fifty of 170 participants (29.4%) dropped out of follow-up by 5 years.
Among the 120 participants who completed the 5-year examination, median change from baseline in visual acuity was -2 letters for participants who had 1 or more long lapse compared with +5 letters for those without a long lapse (P = .02).
After multivariable adjustment, the odds ratio (95% CI) for baseline associations with 1 or more long lapse was 1.21 (1.03-1.43) for each 5-letter decrement in visual acuity score, 2.19 (1.09-4.38) for neovascularization of the disc and elsewhere, and 3.48 (1.38-8.78) for no prior laser treatment for diabetic macular edema.

CONCLUSION: Over 5 years, approximately half of the participants assigned to ranibizumab for PDR had a long lapse in care despite substantial effort by the DRCR Retina Network to facilitate timely completion of examinations.

DOI: 10.1001/jamaophthalmol.2021.4103
PMCID: PMC8532036
PMID: 34673898

3. Graefes Arch Clin Exp Ophthalmol. 2021 Dec 21. doi: 10.1007/s00417-021-05518-0. Online ahead of print.

MANIFESTATIONS OF INTRAOCULAR INFLAMMATION OVER TIME IN PATIENTS ON BROLUCIZUMAB FOR NEOVASCULAR AMD.

Khoramnia R(1)(2), Figueroa MS(3), Hattenbach LO(4), Pavesio CE(5), Anderesi M(6), Schmouder R(7), Chen Y(7), de Smet MD(8).

PURPOSE: To describe the adverse events associated with brolucizumab, in particular the sequence of intraocular inflammation (IOI), retinal vasculitis (RV), and/or retinal vascular occlusion (RO).

METHODS: This was an unmasked post hoc analysis of the randomized HAWK/HARRIER clinical trials. Patients with neovascular AMD in the brolucizumab arms of the trials were included. IOI-related adverse events reported by study investigators were analyzed to determine early signs and the time course of IOI-related adverse events, using a subgroup of patients with definite/probable IOI cases identified in an independent unmasked post hoc review by an external safety review committee. A limited literature review on IOI following anti-VEGF therapy was also conducted.

RESULTS: Among 50 patients with definite/probable IOI cases identified by the safety review committee, 12 had RV or RO adverse events reported by the investigators. For 6 of 12, IOI (other than RV) was reported before RV or RO. The duration from the first IOI adverse event to the first RV or RO adverse event ranged from 16 to 171 days for 5 patients and was 553 days for 1 patient. Four of the 6 patients received ≥ 1 brolucizumab injection on or after the date of the first IOI adverse event and before the first RV or RO adverse event.

CONCLUSIONS: IOI may precede RV or RO in some patients treated with brolucizumab.

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PMID: 34932153

4. Retina. 2021 Dec 13. doi: 10.1097/IAE.0000000000003388. Online ahead of print.

NON-INVASIVE DIAGNOSTIC STRATEGY OF OCULAR TOXOCARIASIS BASED ON CLINICAL FEATURES.

Jiang Z(1), Sun L, Huang L, Li S, Hou A, Zheng S, Ding X.

PURPOSE: To develop a non-invasive diagnostic strategy based on the clinical manifestations of ocular toxocariasis (OT), and evaluate its sensitivity and specificity.

METHODS: Patients with unilateral OT-like lesions were enrolled retrospectively and classified into OT and non-OT groups according to the immunologic diagnosis criterion of anti-OT IgG. Nine clinical manifestations were recorded and compared between groups. Among them, the retrolental membrane (RM), branch-like vitreous strands (BVS), and retinal granulomas (RG) were the most common, which were further classified into three categories, including at least 1 out of 3 signs, at least 2 out of 3 signs, and all 3 signs positive. Diagnostic sensitivity and specificity were calculated for each strategy.

RESULTS: There were 105 immunologically confirmed patients with OT and 70 patients with non-OT uveitis/vitreoretinopathy. RG, RM, and BVS were significantly more frequent in OT patients than in non-OT patients. At least 1 of 3 signs positive strategy showed the highest sensitivity (100.0%) but the lowest specificity (62.0%). At least 2 out of 3 signs positive strategies showed 80.0% sensitivity and 94.3% specificity. All 3 signs positive strategies had the lowest sensitivity (46.7%) and the highest specificity (100.0%). The cutoff point of this revealed an area under the curve of 0.85 and a 95% confidence interval of 0.79 to 0.91.

CONCLUSION: A comprehensive strategy based on at least 2 out of 3 positive signs showed excellent sensitivity and specificity, and could serve as a non-invasive and fast screening strategy for the clinical diagnosis of OT.

DOI: 10.1097/IAE.0000000000003388
PMID: 34923511

5. Biology (Basel). 2021 Dec 15;10(12):1328. doi: 10.3390/biology10121328.

THERAPEUTIC EFFECTS OF FENOFIBRATE NANO-EMULSION EYE DROPS ON RETINAL VASCULAR LEAKAGE AND NEOVASCULARIZATION.

Huang L(1)(2), Liang W(2), Zhou K(2), Wassel RA(3), Ridge ZD(3), Ma JX(2), Wang B(1).

Macular edema caused by retinal vascular leakage and ocular neovascularization are the leading causes of severe vision loss in diabetic retinopathy (DR) and age-related macular degeneration (AMD) patients. Oral administration of fenofibrate, a PPARα agonist, has shown therapeutic effects on macular edema and retinal neovascularization in diabetic patients. To improve the drug delivery to the retina and its efficacy, we have developed a nano-emulsion-based fenofibrate eye drop formulation that delivered significantly higher amounts of the drug to the retina compared to the systemic administration, as measured by liquid chromatography-mass spectrometer (LC-MS).

The fenofibrate eye drop decreased leukocytes adherent to retinal vasculature and attenuated overexpression of multiple inflammatory factors in the retina of very low-density lipoprotein receptor knockout (Vldlr-/-) mice, a model manifesting AMD phenotypes, and streptozotocin-induced diabetic rats. The fenofibrate eye drop also reduced retinal vascular leakage in these models. The laser-induced choroidal neovascularization was also alleviated by the fenofibrate eye drop. There were no detectable ocular toxicities associated with the fenofibrate eye drop treatment. These findings suggest that fenofibrate can be delivered efficiently to the retina through topical administration of the nano-emulsion eye drop, which has therapeutic potential for macular edema and neovascularization.

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Conflict of interest statement: Ronald A Wassel is an inventor of the patent covering the formulation of the nano-emulsion. Jian-Xing Ma is a founder of EyeCro, LLC.