Retina Roundup

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1. Int J Retina Vitreous. 2023 Jun 18;9(1):36.doi: 10.1186/s40942-023-00471-y

EVALUATION OF VISUAL ACUITY IN DRY AMD PATIENTS AFTER MICROCURRENT ELECTRICAL STIMULATION

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Background: To assess micro current to improve vision for dry age-related macular degeneration. Dry age-related macular degeneration is a major cause of blindness, disability, and severe erosion of quality of life, throughout the world. Beyond nutritional supplementation, there is no approved therapy.

Methods: This was a prospective randomized sham controlled clinical trial for participants with confirmed dry AMD with documented visual loss. Participants were randomized three to one, to receive trans palpebral external micro current electrical stimulation with the MacuMira device. The Treatment group received four treatments in the first two weeks, and two further treatments at weeks 14 and 26. Differences in BCVA and contrast sensitivity (CS) were estimated with mixed-effects repeated measures analysis of variance.

Results: Change of visual acuity with ETDRS assessment of number of letters read (NLR) and contrast sensitivity at week 4 and 30, compared to the first visit, between 43 treatment and 19 sham control participants. The Sham Control group had NLR of 24.2 (SD 7.1) at baseline, 24.2 (SD 7.2) at 4 weeks, and 22.1 (SD7.4) at 30 weeks. The Treatment group had NLR of 19.6 (SD 8.9) at baseline, 27.6 (SD 9.1) at 4 weeks, and 27.8 (SD 8.4) at 30 weeks. The change in NLR from baseline in the Treatment compared to the Sham control group was 7.7 (95% CI 5.7, 9.7, $p < 0.001$) at 4 weeks and 10.4 (95% CI 7.8, 13.1, $p < 0.001$) at 30 weeks. There were similar benefits in CS.

Conclusions: This pilot study of trans palpebral microcurrent demonstrated improved visual measures and is very encouraging as a potential treatment for dry AMD.

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2. Cochrane Database Syst Rev. 2023 Jun 13;6(6):CD013318.

FENOFIBRATE FOR DIABETIC RETINOPATHY

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Background: Diabetic retinopathy (DR) remains a major cause of sight loss worldwide, despite new therapies and improvements in the metabolic control of people living with diabetes. Therefore, DR creates a physical and psychological burden for people, and an economic burden for society. Preventing the development and progression of DR, or avoiding the occurrence of its sight-threatening complications is essential, and must be pursued to save sight. Fenofibrate may be a useful strategy to achieve this goal, by reversing diabetes' effects and reducing inflammation in the retina, as well as improving dyslipidaemia and hypertriglyceridemia.

Objectives: To investigate the benefits and harms of fenofibrate for preventing the development and progression of diabetic retinopathy in people with type 1 (T1D) or type 2 diabetes (T2D), compared with placebo or observation.

Search methods: We searched CENTRAL, MEDLINE, Embase, and three trials registers (February 2022).

Selection criteria: We included randomised controlled trials (RCTs) that included people with T1D or T2D, when these compared fenofibrate with placebo or with observation, and assessed the effect of fenofibrate on the development or progression of DR (or both).

Data collection and analysis: We used standard Cochrane methods for data extraction and analysis. Our primary outcome was progression of DR, a composite outcome of 1) incidence of overt retinopathy for participants who did not have DR at baseline, or 2) advancing two or more steps on the Early Treatment Diabetic Retinopathy Study (ETDRS) severity scale for participants who had any DR at baseline (or both), based on the evaluation of stereoscopic or non-stereoscopic fundus photographs, during the follow-up period. Overt retinopathy was defined as the presence of any DR observed on stereoscopic or non-stereoscopic colour fundus photographs. Secondary outcomes included the incidence of overt retinopathy, reduction in visual acuity of participants with a reduction in visual acuity of 10 ETDRS letters or more, proliferative diabetic retinopathy, and diabetic macular oedema; mean vision-related quality of life, and serious adverse events of fenofibrate. We used GRADE to assess the certainty of evidence.

Main results: We included two studies and their eye sub-studies (15,313 participants) in people with T2D. The studies were conducted in the US, Canada, Australia, Finland, and New Zealand; follow-up period was four to five years. One was funded by the government, the other by industry. Compared to placebo or observation, fenofibrate likely results in little to no difference in progression of DR (risk ratio (RR) 0.86; 95% confidence interval (CI) 0.60 to 1.25; 1 study, 1012 participants; moderate-certainty evidence) in a population with and without overt retinopathy at baseline. Those without overt retinopathy at baseline showed little or no progression (RR 1.00, 95% CI 0.68 to 1.47; 1 study, 804 participants); those with overt retinopathy at baseline found that their DR progressed slowly (RR 0.21, 95% CI 0.06 to 0.71; 1 study, 208 people; test for interaction P = 0.02). Compared to placebo or observation, fenofibrate likely resulted in little to no difference in either the incidence of overt retinopathy (RR 0.91; 95% CI 0.76 to 1.09; 2 studies, 1631 participants; moderate-certainty evidence); or the incidence of diabetic macular oedema (RR 0.39; 95% CI 0.12 to 1.24; 1 study, 1012 participants; moderate-certainty evidence). The use of fenofibrate increased severe adverse effects (RR 1.55; 95% CI 1.05 to 2.27; 2 studies, 15,313 participants; high-certainty evidence). The studies did not report on incidence of a reduction in visual acuity of 10 ETDRS letters or more, incidence of proliferative diabetic retinopathy, or mean vision-related quality of life.

Conclusions: Current, moderate-certainty evidence suggests that in a mixed group of people with and without overt retinopathy, who live with T2D, fenofibrate likely results in little to no difference in progression of diabetic retinopathy. However, in people with overt retinopathy who live with T2D, fenofibrate likely reduces the progression. Serious adverse events were rare, but the risk of their occurrence was increased by the use of fenofibrate. There is no evidence on the effect of fenofibrate in people with T1D. More studies, with larger sample sizes, and participants with T1D are needed. They should measure outcomes that are important to people with diabetes, e.g. change in vision, reduction in visual acuity of 10 ETDRS letters or more, developing proliferative diabetic retinopathy; and evaluating the requirement of other treatments, e.g. injections of anti-vascular endothelial growth factor therapies, steroids.

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3. Retina 2023 Jun 9.10.1097/IAE.0000000000003840. Online ahead of print.

LOW-DOSE SUPPLEMENTATION WITH RETINOL IMPROVES RETINAL FUNCTION IN EYES WITH AGE-RELATED MACULAR DEGENERATION BUT WITHOUT RETICULAR PSEUDODRUSEN

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Aims: To determine the functional impact of oral Vitamin A supplementation in patients with intermediate age-related macular degeneration (iAMD) with and without reticular pseudodrusen (RPD) demonstrating dysfunction in dark adaptation (DA).

Methods: Five patients with iAMD and without RPD (AMD group; mean ± SD age 78.0 ± 4.7 years) and seven with RPD (RPD group; age 74.1 ± 11.2 years) were supplemented with 16,000 IU of Vitamin A palmitate for 8 weeks. Assessment at baseline, 4, 8 and 12 weeks included scotopic thresholds, dark adaptation, best-corrected and low luminance visual acuities and the low-luminance quality of life questionnaire.

Results: In the linear mixed model, RIT improved significantly in the AMD group (mean[95% CI] change -1.1 min [-1.8; -0.5] after 4 weeks ($p<0.001$) and -2.2 min[-2.9; 1.6] after 8 weeks of Vitamin A supplementation ($p<0.001$). The DA cone plateau also significantly improved (i.e. more sensitive cone threshold) at 4 and 8 weeks ($p=0.026$ and $p=0.001$). No other parameters improved in the AMD group and there was no significant improvement in any parameter in the RPD group despite significantly elevated serum Vitamin A levels measurable in both groups after supplementation ($p=0.024$ and $p=0.013$).

Conclusions: Supplementation with 16,000IU Vitamin A, a lower dose than used in previous studies, partially overcomes the pathophysiologic functional changes in AMD eyes. The lack of improvement in the RPD group may indicate structural impediments to increasing vitamin A availability in these patients, and/or may reflect the higher variability observed in the functional parameters for this group.

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ACCURACY OF NEW INTRAOCULAR LENS CALCULATION FORMULAE IN EYES UNDERGOING SILICONE OIL REMOVAL/PARS PLANA VITRECTOMY-CATARACT SURGERY

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Purpose: To investigate the performance of novel intraocular lens (IOL) calculation formulae (Barrett Universal II [BUII], Emmetropia Verifying Optical [EVO], and Kane) and conventional formulae (Haigis, Hoffer Q, Holladay 1, and SRK/T) in patients who underwent pars plana vitrectomy (PPV) or silicone oil removal (SOR) combined with cataract surgery.

Methods: In total, 301 eyes from 301 patients underwent PPV/SOR with concomitant cataract surgery were enrolled and divided into four groups according to preoperative diagnosis: silicone oil-filled eyes after PPV, epiretinal membrane, primary retinal detachment (RD), and macular hole.

Results: BUII exhibited the smallest mean absolute error (MAE) (0.65 diopters [D]) and median absolute error (MedAE) (0.39 D) in total. In patients with RD, each formula exhibited the worst refractive outcomes in diverse vitreoretinal pathologies (P<.01), and no difference in accuracy between the seven formulas was observed (P=.075). For long eyes, the second linear (WK2) version of the Wang-Koch adjustment significantly reduced the MedAE for Holladay 1 and SRK/T (P<.001 and P=.019).

Conclusion: In combined surgery, both new and conventional formulas using WK2 adjustment demonstrated satisfactory performance, with BUII exhibiting the best overall performance. However, in patients with RD, all seven formulas showed less favorable performance.

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5. Am J Ophthalmol 2023 Jul;251:189-196.

LONGITUDINAL ANALYSIS OF OCULAR MANIFESTATION AND INTERLEUKIN DURING INTRAVITREAL TREATMENT OF VITREORETINAL LYMPHOMA WITH METHOTREXATE

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Purpose: To explore the trend of ocular manifestations and interleukin (IL) during the treatment of vitreoretinal lymphoma (VRL) and to evaluate the potential effects of different intravitreal administration schedules on the therapeutic response.

Design: Interventional comparative nonrandomized clinical study.

Methods: Patients diagnosed with VRL between January 2011 and January 2022 were included. Intravitreal methotrexate (MTX) injections consisting of induction, consolidation, and maintenance were scheduled. At baseline and each visit, ocular manifestations and IL in aqueous humor were recorded. Effects of the variations (eg frequency and number) in the injection schedule on the therapeutic response were analyzed.

Results: Fifty-eight eyes of 33 patients were treated with intravitreal MTX chemotherapy. A mean ± standard deviation of 9 ± 3 injections were given; 52 eyes achieved complete remission (CR). IL-10, keratic precipitates, and subretinal lesions correlated well with the course of treatment (all $P < .001$). Initial injection given twice weekly was correlated with a higher rate of CR (36/36) than given once weekly or less frequently (16/22; $P = .011$). Ocular progression occurred in 13 eyes of 8 patients. The completion of schedule was correlated with PFS (induction + consolidation + maintenance: 547 [335-874] days; induction + consolidation: 355 [322-831] days; induction only: 147 [116-187.5] days; $P < .001$). IL-10 >50 pg/mL was a feasible threshold for the detection of ocular relapse (sensitivity 100.0%, specificity 95.1%).

Conclusion: Keratic precipitates, subretinal lesions, and IL-10 could serve as indicators for therapeutic response. Intensive initial administration and adequate injection numbers would help to improve the response and prognosis. IL-10 >50 pg/mL could help detect ocular relapse.

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