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FEATURED ARTICLE

What did we learn in 35 years of research on nutrition and supplements for age-related macular degeneration: a systematic review.

Acta Ophthalmology. 2022 Jun 13.

Pameijer EM, Heus P, Damen JAA, Spijker R, Hooft L, Ringens PJ, Imhof SM, van Leeuwen R.

The aim of this paper is to summarize all available evidence from systematic reviews, randomized controlled trials (RCTs) and comparative nonrandomized studies (NRS) on the association between nutrition and antioxidant, vitamin, and mineral supplements and the development or progression of age-related macular degeneration (AMD). The Cochrane Database of Systematic Reviews, Cochrane register CENTRAL, MEDLINE and Embase were searched and studies published between January 2015 and May 2021 were included. The certainty of evidence was assessed according to the GRADE methodology. The main outcome measures were development of AMD, progression of AMD, and side effects. We included 7 systematic reviews, 7 RCTs, and 13 NRS. A high consumption of specific nutrients, i.e. β-carotene, lutein and zeaxanthin, copper, folate, magnesium, vitamin A, niacin, vitamin B6, vitamin C, docosahexaenoic acid, and eicosapentaenoic acid, was associated with a lower risk of progression of early to late AMD (high certainty of evidence). Use of antioxidant supplements and adherence to a Mediterranean diet, characterized by a high consumption of vegetables, whole grains, and nuts and a low consumption of red meat, were associated with a decreased risk of progression of early to late AMD (moderate certainty of evidence). A high consumption of alcohol was associated with a higher risk of developing AMD (moderate certainty of evidence). Supplementary vitamin C, vitamin E, or β-carotene were not associated with the development of AMD, and supplementary omega-3 fatty acids were not associated with progression to late AMD (high certainty of evidence). Research in the last 35 years included in our overview supports that a high intake of specific nutrients, the use of antioxidant supplements and adherence to a Mediterranean diet decrease the risk of progression of early to late AMD.

DOI: 10.1111/aos.15191

BIOMARKERS

Relationship between soluble protein ST2 (sST2) levels and microvascular complications in a cohort of patients with type 1 diabetes.

Endocrinology Diabetes and Nutrition 2022 May.

Forga L, López-Andrés N, Tamayo I, Fernández-Celis A, García-Mouriz M, Goñi MJ.

Aim: To determine the association and the prognostic value of soluble ST2 (sST2) levels in the development of diabetic retinopathy (DR), diabetic macular oedema (DMO) or diabetic nephropathy (DN), in a cohort of patients with type 1 diabetes (T1D).

Methods: A total of 269 individuals with T1D (154 males and 115 females) were recruited. The overall mean age was 43.2±14.9 years, and the diabetes duration was 17.1±12.1 years. Levels of sST2 in serum were evaluated, and the presence as well as the degree of DR, DMO and DN was recorded. Additionally, other clinical and analytical parameters including demographic variables were recovered from patients' electronic health record. Ten years later, the presence and stage of DR, DMO and DN were again recorded under the same criteria. The association between previously mentioned parameters with DR and DN was analysed by univariate and multivariate logistic regression. The variables in the final multivariate models were adjusted from complete models via backward elimination and maintained only when significant.

Results: An increase of 10ng/ml in the levels of sST2 was associated with a 1.50 (1.02-2.19) and 1.48 (1.05-2.08) prevalence odds ratio (OR) in DMO and DR, respectively. There was no association between sST2 levels and DN. Meanwhile, sST2 levels did not display a prognostic effect in any of the microangiopathic diabetic complications studied.

Conclusions: Levels of sST2 are associated with the presence of DR and DMO, they do not seem to be predictive for the development or deterioration of DR, DMO or DN.

DOI: 10.1016/j.endien.2021.02.006

Exploring Reticular Pseudodrusen Extent and Impact on Mesopic Visual Sensitivity in Intermediate Age-Related Macular Degeneration.

Investigative Ophthalmology and Vision Science 2022 Jun 1.

Kumar H, Guymer RH, Hodgson LAB, Hadoux X, Wu Z.

Purpose: To explore the impact of the extent of reticular pseudodrusen (RPD) on mesopic visual sensitivity in individuals with intermediate age-related macular degeneration (AMD).

Methods: In total, 570 eyes from 285 participants with bilateral large drusen underwent microperimetry testing to assess the visual sensitivity of the central 3.6-mm region and multimodal imaging to determine the extent of RPD in the central 20° × 20° region (at the eye level). Mean visual sensitivity within five sectors in the central 3.6-mm region sampled on microperimetry and the extent of RPD in these sectors were derived. Linear mixed models were used to examine the association between the extent of RPD on overall mean visual sensitivity and sector-based mean sensitivity.

Results: An increasing extent of RPD at the eye level and within sectors was associated with a significant reduction in overall and sector-based mean sensitivity, respectively ($P < 0.001$ for both). However, when both RPD parameters were considered together in a multivariable model, only an increasing extent of RPD at the eye level ($P < 0.001$) and not within each sector ($P = 0.178$) was independently associated with reduced sector-based mean sensitivity.

Conclusions: Mesopic visual sensitivity is generally reduced in eyes with large drusen and coexistent RPD compared to eyes without RPD, with greater reductions with an increasing extent of RPD. However, reduced

sector-based visual sensitivities are explained by the overall extent of RPD present, rather than their extent within the sector itself. These findings suggest that there are generalized pathogenic changes in eyes with RPD accounting for the observed mesopic visual dysfunction.

DOI: 10.1167/iovs.63.6.14

EPIDEMIOLOGY

Diabetic Retinopathy and Diabetic Macular Edema in People With Early-Onset Diabetes.

ClinIcal Diabetes. 2022 Spring.

Reddy NG, Venkatesh R, Jayadev C, Gadde SGK, Agrawal S, Mishra P, Yadav NK, Chhablani J.

This study examined the clinical profile, treatment profile, and vision outcomes of people ≤40 years of age with diabetes and diabetic macular edema (DME). Within this age-group, the prevalence of center-involving DME was 16%, with 74% of eyes showing cystoid edema, 37% showing spongiform edema, and 41% having neurosensory detachment. Longer diabetes duration (P = 0.001) and greater severity of diabetic retinopathy (P <0.001) were associated with DME prevalence. Thus, regular and more frequent follow-up, as well as early and aggressive treatment of diabetic eye disease, are required in people diagnosed early with diabetes.

DOI: 10.2337/cd21-0110

GENETICS

Evaluating a Causal Relationship between Complement Factor I Protein Level and Advanced Age-Related Macular Degeneration Using Mendelian Randomization.

Ophthalmology Science. 2022 Jun.

Jones AV, MacGregor S, Han X, Francis J, Harris C; SCOPE Study group, Kavanagh D, Lotery A, Waheed N.

Importance: Risk of advanced age-related macular degeneration (AAMD) is associated with rare genetic variants in the gene encoding Complement factor I (CFI), which is associated with lower circulating CFI protein levels, but the nature of the relationship is unclear.

Objective: Can genetic factors be used to infer whether low circulating CFI is associated with AAMD risk? DESIGN: Two-sample inverse variance weighted Mendelian Randomisation (MR) was used to evaluate evidence for a relationship between CFI levels and AAMD risk, comparing CFI levels from genetically predefined subsets in AAMD and control cohorts.

Setting: Published genetic and proteomic data was combined with data from cohorts of Geographic Atrophy (GA) patients in a series of MR analyses.

Participants: We derived genetic instruments for systemic CFI level in 3,301 healthy European participants in the INTERVAL study. To evaluate a genetic causal odds ratio (OR) for the effect of CFI levels on AAMD risk, we used results from a genome-wide association study of 12,711 AAMD cases and 14,590 European controls from the International AMD Genomics Consortium (IAMDGC), and CFI levels from patients entered into the research studies SCOPE and SIGHT.

Results: We identified one common CFI variant rs7439493 which was strongly associated with low CFI level, explaining 4.8% of phenotypic variance. Using rs7439493 our MR analysis estimated that AAMD odds increased per standard deviation (SD) decrease in CFI level; OR 1.47 (95% confidence interval (CI)

1.30-1.65, P=2.1×10-10). We identified one rare variant (rs141853578 encoding p.Gly119Arg) which was genome-wide significantly associated with CFI levels after imputation; based on this, a 1 SD decrease in CFI leads to increased AAMD odds of 1.79 (95% CI 1.46-2.19, P=1.9×10-8). The rare variant rs141853578 explained a further 1.7% of phenotypic variance. To benchmark the effect of low CFI levels on AAMD odds using a CFI-specific proteomic assay, we estimated the effect using CFI levels from 24 rs141853578 positive GA patients; each 1 SD (3.5µg/mL) reduction in CFI was associated with 1.67 fold increased odds of AAMD (95% CI 1.40-2.00, P=1.85×10-8).

Conclusion And Relevance: Excellent concordance in direction and effect size derived from rare and common variant calculations provide good genetic evidence for a potentially causal role of lower CFI level increasing AAMD risk.

DOI: 10.1016/j.xops.2022.100146

A proteogenomic signature of age-related macular degeneration in blood.

Nature Communications. 2022 Jun 13.

Emilsson V, Gudmundsson EF, Jonmundsson T, Jonsson BG, Twarog M, Gudmundsdottir V, Li Z, Finkel N, Poor S, Liu X, Esterberg R, Zhang Y, Jose S, Huang CL, Liao SM, Loureiro J, Zhang Q, Grosskreutz CL, Nguyen AA, Huang Q, Leehy B, Pitts R, Aspelund T, Lamb JR, Jonasson F, Launer LJ, Cotch MF, Jennings LL, Gudnason V, Walshe TE.

Age-related macular degeneration (AMD) is one of the most common causes of visual impairment in the elderly, with a complex and still poorly understood etiology. Whole-genome association studies have discovered 34 genomic regions associated with AMD. However, the genes and cognate proteins that mediate the risk, are largely unknown. In the current study, we integrate levels of 4782 human serum proteins with all genetic risk loci for AMD in a large population-based study of the elderly, revealing many proteins and pathways linked to the disease. Serum proteins are also found to reflect AMD severity independent of genetics and predict progression from early to advanced AMD after five years in this population. A two-sample Mendelian randomization study identifies several proteins that are causally related to the disease and are directionally consistent with the observational estimates. In this work, we present a robust and unique framework for elucidating the pathobiology of AMD.

DOI: 10.1038/s41467-022-31085-x

REVIEW

The influence of the macular carotenoids on women's eye and brain health.

Nutritional Neuroscience 2022 Jun 11.

Introduction: The mortality-morbidity paradox refers to the inconsistency in survival and disease between males and females: females live longer but tend to suffer greater age-related disease and disability. Many aspects of the latter can be targeted by lifestyle interventions, such as changes in dietary behavior.

Methods: The relevant literature is reviewed.

Conclusion: Dietary intake of the pigmented carotenoids appears to be particularly important for issues such as visual and cognitive loss. This may be due to the highly selective presence of a fraction of carotenoids, namely lutein (L) and zeaxanthin (Z), in specific tissues of the eye and brain. At those sites, L and Z have been shown to directly improve function and prevent central nervous system degeneration. On the palliative side, retinal LZ reduce glare disability, discomfort and photostress, improve chromatic contrast and visual range (e.g., the ability to see through blue atmospheric haze). These effects on input reflect changes in neural output such as improved visual processing speed, problem solving, memory and executive function (presumably due, also, to local effects in areas such as the hippocampus and frontal cortex). These effects on function throughout the central nervous system are mirrored by effects on disease

progression. As potent antioxidants/anti-inflammatory agents, and "blue-blockers" within the retina, the pigments prevent loss that precedes neurodegenerative diseases such as age-related macular degeneration and some forms of dementia.

DOI: 10.1080/1028415X.2022.2084125

DIAGNOSIS AND IMAGING

Evaluation of a self-imaging SD-OCT system designed for remote home monitoring.

BMC Ophthalmology 2022 Jun 10.

Kim JE, Tomkins-Netzer O, Elman MJ, Lally DR, Goldstein M, Goldenberg D, Shulman S, Benyamini G, Loewenstein A.

Purpose: To compare identification rates of retinal fluid of the Notal Vision Home Optical Coherence Tomography (OCT) device (NVHO) when used by people with age-related macular degeneration (AMD) to those captured by a commercial OCT.
Methods: Prospective, cross-sectional study where patients underwent commercial OCT imaging followed by self-imaging with either the NVHO 2.5 or the NVHO 3 in clinic setting. Outcomes included patients' ability to acquire analyzable OCT images with the NVHO and to compare those with commercial images.
Results: Successful images were acquired with the NVHO 2.5 in 469/531 eyes (88%) in 264/290 subjects (91%) with the mean (SD) age of 78.8 (8.8); 153 (58%) were female with median visual acuity (VA) of 20/40. In the NVHO 3 cohort, 69 eyes of 45 subjects (93%) completed the self-imaging. Higher rates of successful imaging were found in eyes with VA ≥ 20/320. Positive percent agreement/negative percent agreement for detecting the presence of subretinal and/or intraretinal fluid when reviewing for fluid in three repeated volume scans were 97%/95%, respectively for the NVHO v3.
Conclusion: Self-testing with the NVHO can produce high quality images suitable for fluid identification by human graders, suggesting the device may be able to complement standard-of-care clinical assessments and treatments.

DOI: 10.1186/s12886-022-02458-z

CASE REPORT

Swept-source optical coherence tomography angiography of retinal occlusive vasculitis following brolucizumab administration: a case report.

BMC Ophthalmology. 2022 Jun 3.

Lee EK, Oh BL, Yoon CK, Park UC.

Background: We present a case of retinal occlusive vasculitis following brolucizumab administration and the first report of optical coherence tomography angiography (OCTA) findings after treatment.

Case Presentation: A 71-year-old man complained of vision loss in the left eye 6 weeks after brolucizumab injection. His visual acuity was counting fingers, and examination revealed 1 + anterior chamber cells with 2 + vitreous cells. Fundus examination demonstrated vitreous haze, retinal whitening, and vascular sheathing. Fluorescein angiography revealed filling defects in the retinal arteries and veins, and OCTA showed extensive capillary nonperfusion. Under the diagnosis of brolucizumab-associated intraocular inflammation (IOI) and retinal occlusive vasculitis, topical, sub-Tenon, and systemic corticosteroids were administered. After the treatment, visual acuity improved to 20/200, and OCTA revealed gradual improvement in capillary dropout; however, with the limited improvement of reperfusion in the perifoveal areas.

Conclusions: Prompt evaluation and intensive corticosteroid treatments are required for brolucizumab-associated IOI. OCTA imaging provides detailed information on microvascular changes in the retinal vascular plexuses in brolucizumab-associated retinal occlusive vasculitis.

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